RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

Vol. 47 NOVEMBER 1946 No. 5

Eosinophilic Granuloma of Bone[1]

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A peculiar destructive granulomatous lesion of bone was first recognized and described independently in 1940 by Otani and Ehrlich (18) and Lichtenstein and Jaffe (14). Lesions of similar type had previously been described by Finzi (6) in 1929, Mignon (16) in 1930, and Schairer (21) in 1938. They did not, however, consider the lesion to be a distinct entity and referred to it as myeloma with prevalence of eosinophils, granulation tumor of bone, and osteomyelitis with eosinophilic reaction, respectively. Lichtenstein and Jaffe's denomination, "eosinophilic granuloma of bone," has been widely accepted. Up to July 1, 1945, 48 acceptable cases were recorded in the literature. To these are added the 5 reported in this paper, making a total of 53 published cases.

ETIOLOGY

The cause of eosinophilic granuloma of bone is as yet unknown. Trauma has been considered significant, but proof of a causative relationship is lacking in most instances. Ziehl-Neelsen stains and guinea-pig inoculation of material from the lesions have failed to demonstrate tubercle bacilli. Other bacteriological examinations have shown no organism to be present with any degree of frequency. At the present time most authors consider the lesion to be of inflammatory type, but a causative organism has not been demonstrated.

SEX AND AGE OF PATIENTS

Of the 53 cases which are reported in the literature (including the present series), 36 were in males and 7 were in females; in 10 cases the sex was not indicated.

The incidence with respect to age at the time when the diagnosis was established by operation or autopsy is shown in Table I.

TABLE I: AGE INCIDENCE

Less than 10 years	20 (37.7%)
10 to 19 years	14 (26.4%)
20 to 29 years	7 (13.2%)
30 to 39 years	3 (5.7%)
40 to 49 years	0
50 to 59 years	2 (3.8%)
Age not stated	7 (13.2%)

The youngest patient was a six-month-old boy, the oldest a fifty-eight-year-old man. As indicated in the tabulation, eosinophilic granuloma is more common in the younger age group, 64 per cent of the cases occurring in those less than twenty years of age. Although most common in childhood, the condition is not limited to children and young adults.

LOCATION OF LESIONS

In the great majority of instances the lesions are confined to bone. Neverthe-

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less, a few instances (15, 22) of extra-osseous eosinophilic granuloma, of which Case 3 in this paper is an example, have been described.

The osseous lesions are usually solitary and involve the bones of the skull or pelvis, the vertebrae, ribs, and long bones. Multiple lesions are, however, not uncommon. The greatest number of lesions in a single case was 25. The lesions were solitary in 36 and multiple in 10 of the 53 recorded cases. In 7 cases the number of bones involved was not stated.

The location of 108 lesions in 46 cases adequately reported with respect to this feature is indicated in Table II.

TABLE II: LOCATION OF LESIONS

	36 Cases with Solitary Lesions		10 Cases with Multiple Lesions	
	Number	Per Cent	Number	Per Cent
Skull	13	36.0	8	11.0
Ribs	6	16.6	24	33.3
Femur	6	16.6	7	9.8
Pelvis	2	5.5	5	7.0
Humerus	2	5.5	7	9.8
Tibia	2	5.5	2	2.8
Radius	1	2.8	0	0
Sternum	1	2.8	0	0
Scapula	1	2.8	2	2.8
Clavicle	1	2.8	0	0
Mandible	1	2.8	4	5.5
Fibula	0	0	2	2.8
Vertebrae	0	0	9	12.5
Face	0	0	2	2.8
TOTAL	36	99.7	72	100.0

SIGNS AND SYMPTOMS

Local and systemic signs and symptoms of slight to moderate degree are present in most instances. Occasionally, however, as in 2 of the present series of 5 cases, the lesions remain quiescent, produce no symptoms, and are discovered only at autopsy. When multiple lesions are present, only one, or a few of them, may give rise to signs or symptoms.

The most common symptoms are pain, swelling of the soft tissues, and tenderness at the site of the lesion. The pain, which varies from slight to severe, may have a duration of a few days to several months. Soft-tissue masses 2 to 4 cm. in diameter may develop over the osseous lesions. Other local signs are muscular spasm and atrophy.

There may be systemic manifestations, including slight fever, anorexia, easy fatigability, headache, and loss of weight. Leukocytosis of slight degree and eosinophilia (4 to 11 per cent) are sometimes noted. The blood sedimentation rate may be increased. Bone-marrow biopsies frequently reveal an increased number of eosinophils. Blood chemical determinations, including cholesterol, are characteristically normal.

ROENTGENOLOGIC FEATURES

X-ray examination reveals a round, oval, or irregularly shaped area of decreased density sharply demarcated from adjacent normal bone. The lesions usually vary from 1 to 4 cm. in diameter. There is no osteoporosis of surrounding bone. Sclerosis of the margins of the lesion has been mentioned in two previous reports and occurred in one of the cases reported in this paper (Case 4, Fig. 11). Periosteal thickening of long bones was noted in 2 cases reported in this paper and in 12 of those previously recorded. Soft-tissue swelling is common in eosinophilic granulomas of the skull and not uncommon in those of ribs and vertebrae. The lesions apparently originate in the medullary portion of the bone. As the lesion grows, the cortex may be decreased in thickness, sometimes perforated, occasionally expanded. Spontaneous pathologic fractures may result at the site of the granuloma (23).

MORPHOLOGY: GROSS AND MICROSCOPIC

In the early stage the lesion is characteristically cystic and hemorrhagic. The cysts vary from less than one to several centimeters in diameter and contain soft, friable, yellowish-brown and red material. The yellow color is due to necrosis or lipid, the red to hemorrhage. In later stages the cysts are replaced by friable pale yellow tissue (rich in lipid) that is softer than adjacent bone. With healing there is replacement by gray connective tissue and finally bone formation.

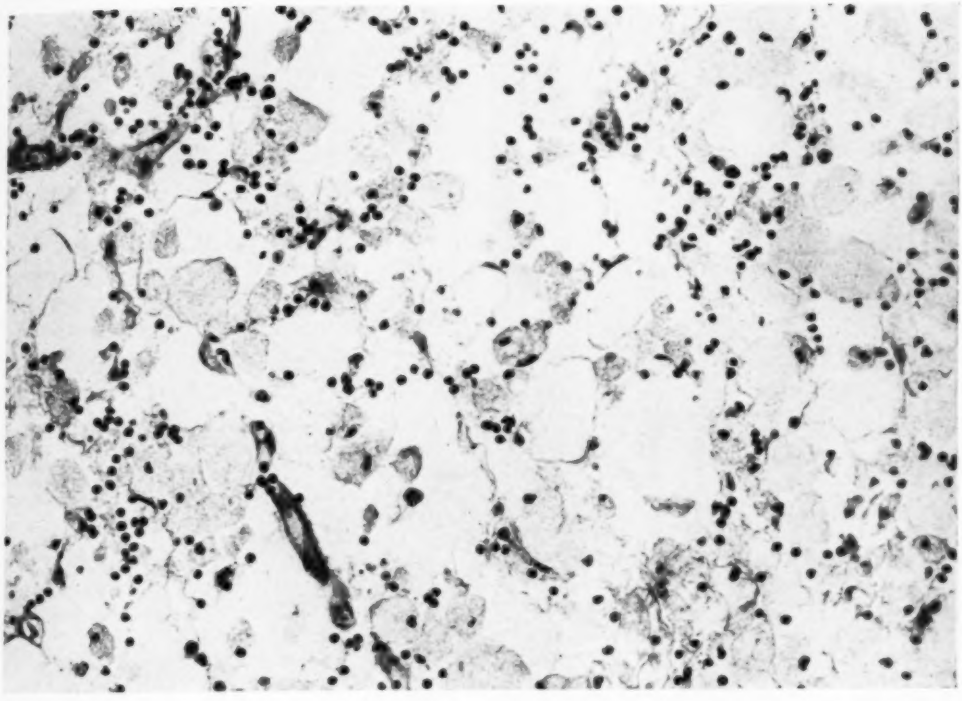


Fig. 1. Case 1. Photomicrograph showing numerous mononuclear "foam" cells and a few lymphocytes. Hematoxylin and eosin. × 312.

The microscopic picture varies in different stages. According to Farber (5), the variations represent stages in evolution of the lesion. In the early destructive (cystic) stage there are foci of necrosis and hemorrhage and a large number of cells. The cells include eosinophilic leukocytes and myelocytes, large mononuclear cells (histiocytes) with granular cytoplasm, lymphocytes, plasma cells, neutrophilic leukocytes, and phagocytic multinucleated giant cells. In the intermediary stage the mononuclear cells have vacuolated (foamy) cytoplasm and eosinophils are few in number or absent. In the late stage there is proliferation of connective tissue and eventually regeneration of bone.

Although at one stage the eosinophil is the predominant and most conspicuous cell, the mononuclear histiocyte (foam cell) is considered the characteristic cell. The presence of these "foam" cells in large numbers has resulted in speculation as to a relationship between eosinophilic granuloma, Letterer-Siwe, and Schüller-Christian's disease. It has been suggested that these three conditions may be the result of an unknown infectious agent, eosinophilic granuloma being the most benign and localized form, limited to bone. The possibility of such a relationship is suggested by (*a*) the similarity of microscopic pictures of all three conditions; (*b*) the development of lesions with the microscopic picture of eosinophilic granuloma in proved cases of Schüller-Christian's disease; (*c*) the occurrence of extra-osseous lesions in instances of eosinophilic granuloma of bone (*e.g.*, in Case 3 of this paper, with involvement of sternum and lymph node).

PROGNOSIS AND TREATMENT

The disease ordinarily runs a course of a few months to a year or more. With or without treatment, the prognosis is usually

Fig. 2. Case 2. Right humerus, showing oval area of decreased density in the lower portion of the shaft.

good, particularly in cases with solitary lesions.

Treatment in the cases reported has consisted of surgical excision, curettage, and irradiation. All three have been effective and apparently relieved symptoms and hastened the disappearance of the soft-tissue swelling and the osseous lesion.

The total dose of radiation has varied from 400 to 500 r (air) to 1,200 to 1,800 r (air). Although the most effective dose and rate of administration have not been determined, radiation is usually given in divided doses of 200 to 300 r daily or even monthly. It seems definite that most cases respond to this type of treatment. Lesions of the skull so treated have shown complete healing in from five to nineteen months.

Because the x-ray appearance of eosinophilic granuloma may be indistinguishable from other inflammatory lesions, multiple myeloma, or metastatic tumor, a biopsy is usually indicated. Thus, in most cases, the treatment of choice is probably either complete curettage or curettage followed by irradiation.

CASE REPORTS

CASE 1: A white female, 36 years of age, was admitted to the hospital complaining of cough, nausea, and vomiting. She had been well until one year prior to hospitalization, at which time she was seen by a physician after she had fainted. Examination revealed the murmurs of mitral and aortic stenosis. Several months later she first noticed a persistent cough. At the time of admission she had signs and symptoms of cardiac failure. She died on her fourth hospital day.

Autopsy (8027, by F. R. Dutra, M.D.) confirmed the diagnosis of rheumatic heart disease and cardiac failure. An unexpected lesion was found in the left sphenoid bone, lateral to the sphenoid sinus. This was 2 cm. in maximum measurement, irregular in shape, sharply circumscribed, softer than adjacent bone, and yellowish orange in color. Microscopic examination (Fig. 1) revealed a large number of mononuclear cells, some lymphocytes, and a small amount of collagenous connective tissue. The mononuclear cells had abundant vacuolated acidophilic cytoplasm and small nuclei. Eosinophils, foci of necrosis, and hemorrhage were absent. The microscopic picture was considered to be typical of the intermediate stage of eosinophilic granuloma.

CASE 2: A white male, aged 58 years, was admitted to University Hospitals of Cleveland, Ohio, on Dec. 7, 1942, complaining of weakness for the previous six to eight weeks. While he was in the hospital, fever, weakness, and generalized aching were the most prominent symptoms. Severe anemia and albuminuria were also noted. The differential blood count showed 2 to 4 per cent eosinophils on many occasions. Roentgenograms of the extremities and pelvis revealed many circular punched-out areas of decreased density, 2 to 4 mm. in diameter. One area of decreased density (Fig. 2) was larger and more sharply defined than the others. This lesion was in the lower portion of the shaft of the right humerus and measured 12 × 10 mm. A sternal biopsy was considered diagnostic of plasma-cell myeloma. The patient died on the 143d hospital day.

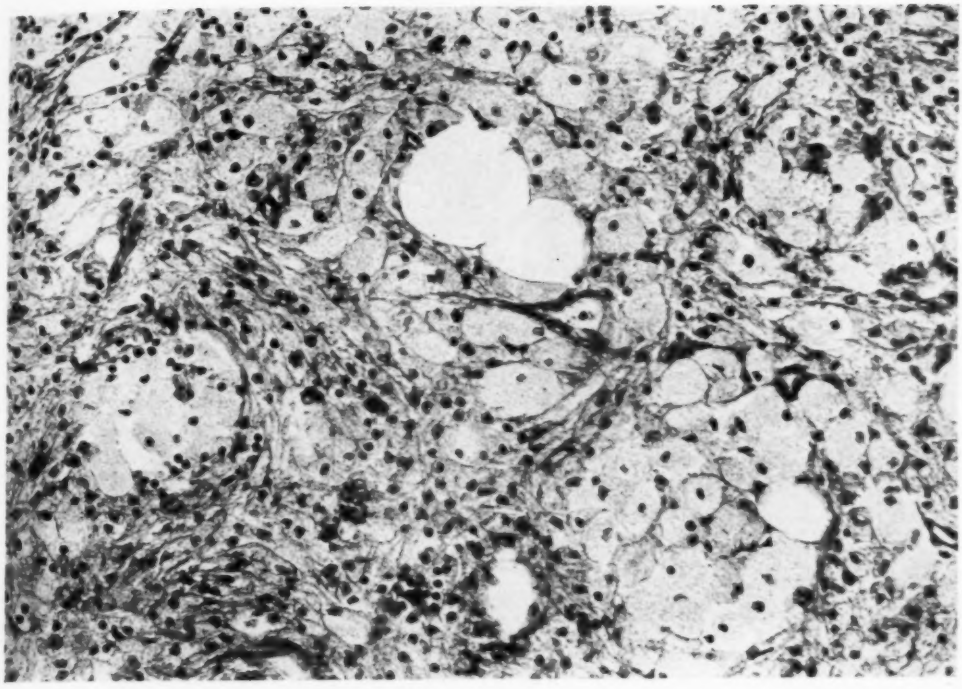


Fig. 3. Case 2. Photomicrograph showing numerous mononuclear "foam" cells and a moderate amount of collagenous connective tissue. Hematoxylin and eosin. × 312.

Autopsy (8118, by O. Eitzen, M.D.) revealed bronchopneumonia as the immediate cause of death. Sections of many lesions from various bones showed the characteristic picture of plasma-cell myeloma. The largest lesion, situated in the right humerus (Fig. 2), had the gross and microscopic features of the intermediate stage of eosinophilic granuloma of bone. The tissue was soft, friable, and dark yellow. Large mononuclear cells with vacuolated (foamy) cytoplasm were abundant, and a moderate amount of collagenous connective tissue was present (Fig. 3). There were no plasma cells or eosinophils in this lesion.

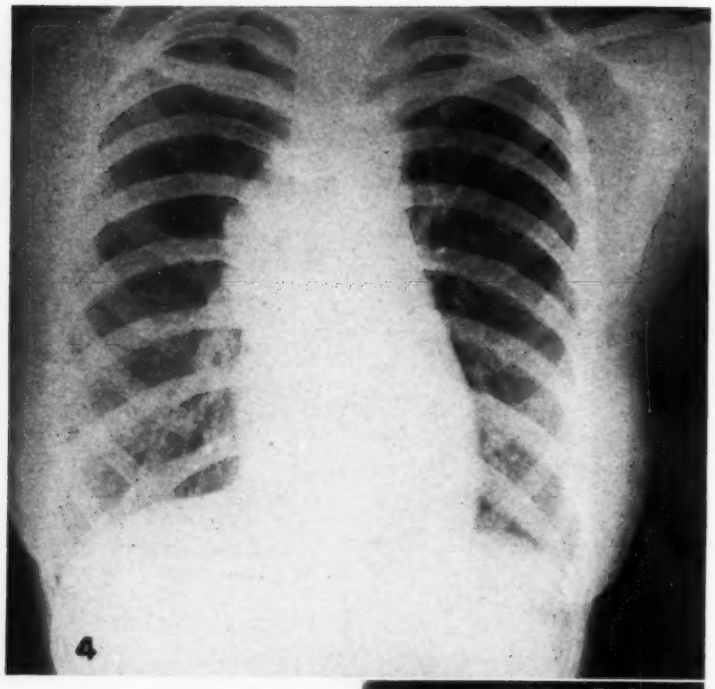
CASE 3: A 17-year-old white female had "a tender lump on the chest." She was admitted to the hospital on Dec. 27, 1943, six weeks after the sternal mass was first noticed. She complained, also, of slight but definite and unusual tiredness. The sternal lesion had been painful continuously for two days before admission to the hospital.

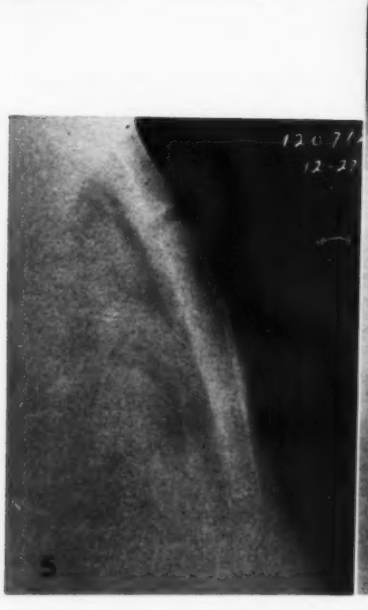
The patient was well developed and well nourished. Her temperature was 37.4° C. There was a firm, rubbery, moderately tender mass at the junction of the right third costal cartilage and sternum. This had a maximum measurement of 5 cm. and was elevated 7 to 8 mm. above adjacent tissue. Several small, discrete, firm, non-tender lymph nodes were palpated superior to the medial portion of the left clavicle.

The laboratory findings were as follows: 7,400 white blood cells (3 per cent eosinophils); 3,870,000 red blood cells; hemoglobin 72 per cent (Sahli); sedimentation rate 1.2 cm. per min.; serum calcium 9.5 mg. per 100 c.c.; serum phosphorus 2.7 mg. per 100 c.c.; serum alkaline phosphatase 10.8 Bodansky units; Kline exclusion test negative.

A postero-anterior chest film (Fig. 4) showed the mediastinum to be widened, measuring 7 cm. In the lateral view of the chest the mediastinal mass appeared along the posterior margin of the sternum. Along the anterior aspect many layers of periosteal new bone formation were evident (Fig. 5). An oval area of destruction, measuring 5 × 3 cm., appeared in the right side of the upper half of the gladiolus on oblique laminagrams (Fig. 6). The edges of this lesion were poorly defined and there was no evidence of sclerosis.

A biopsy was performed on Dec. 28, 1943. The sternal mass consisted of soft, friable, yellowish-gray tissue. The surgeon considered it to be a tuberculous lesion with caseation necrosis. Microscopic examination showed a richly cellular lesion with small foci of necrosis (Fig. 7). Eosinophilic and neutrophilic leukocytes were abundant. There were also many lymphocytes, large mononuclear





Figs. 4–6. Case 3.

Fig. 4. Postero-anterior chest film of Dec. 27, 1943, showing abnormal shadows along the right side of the superior mediastinum. The width of the mediastinum is 7 cm. The lateral chest film showed the mass near the inner table of the sternum.

Fig. 5. A lateral view showing several layers of periosteal new bone along the anterior cortex of the sternum. The inner cortex is also thickened.

Fig. 6. Laminagram made in December 1943, showing a 5 × 3 cm. destructive lesion of the right side of the upper half of the gladiolus of the sternum. The margins of the bone defect are poorly defined. There is no sclerosis.

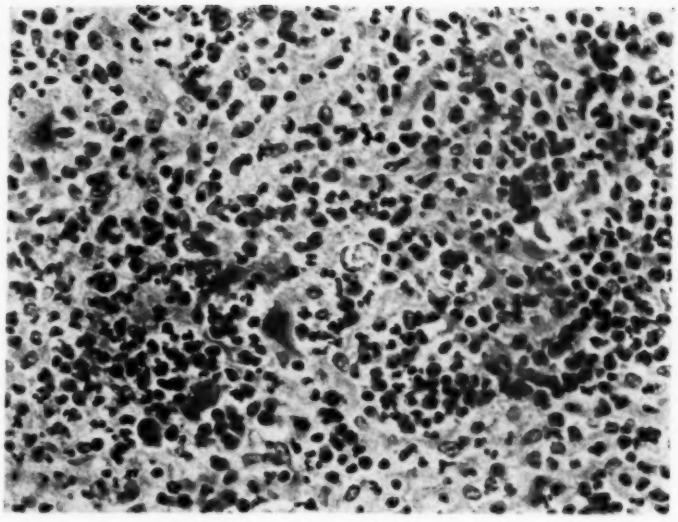


Fig. 7. Case 3. Section of tissue from sternal lesion showing numerous eosinophils, large mononuclear cells, and atypical multinucleated giant cells. Hematoxylin and eosin. × 298.

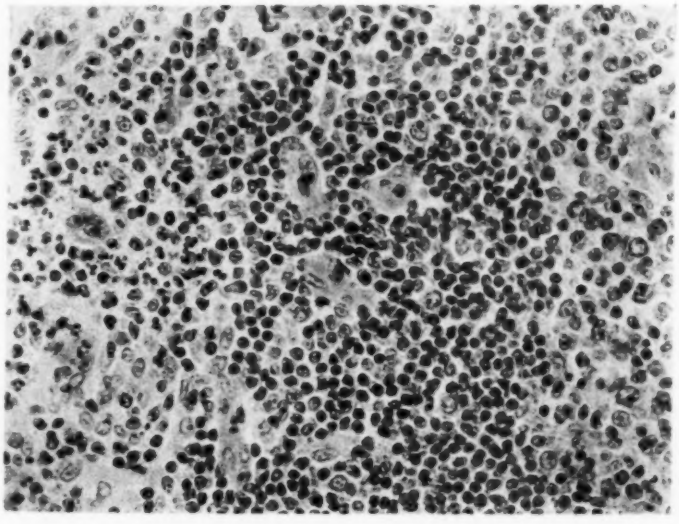


Fig. 8. Case 3. Section of axillary lymph node, illustrating normal lymphoid tissue, eosinophils, mononuclear and multinuclear cells. Hematoxylin and eosin. × 298.

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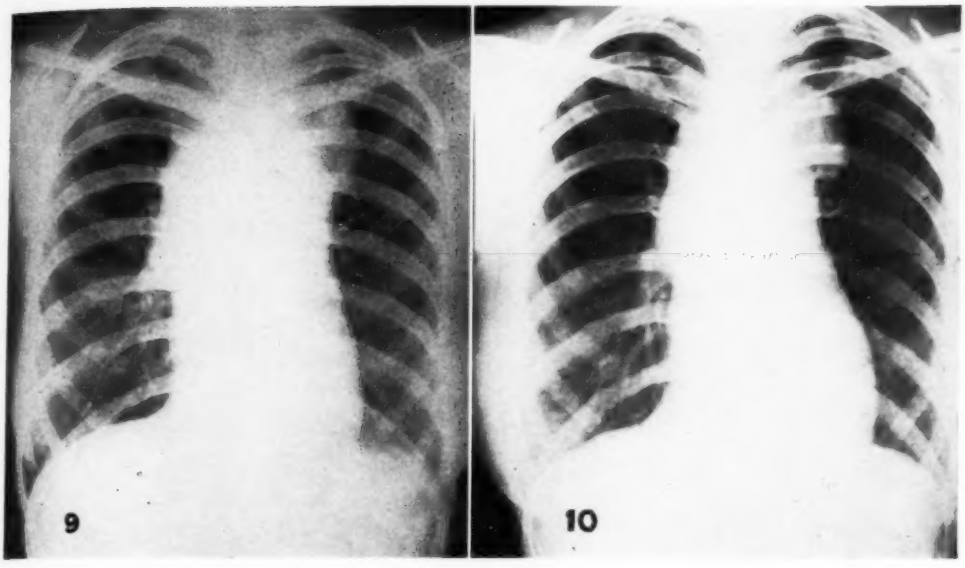


Figs. 9 and 10. Case 3.

Fig. 9. Postero-anterior chest film made in January 1945. The mediastinal mass measures 12.4 cm. in width and 14.0 cm. in length.

Fig. 10. Postero-anterior chest film of September 1945, showing marked enlargement of the mediastinum above the aortic knob. The mass was 11 cm. in its transverse diameter. Lateral chest films showed the shadows to extend to the upper pole of the hilum of the left lung. They probably represent enlarged lymph nodes.

cells, and spindle-shaped fibroblasts. Multinuclear giant cells with large and vesicular nuclei were also present. The unusually large number of eosinophils, the features of the giant cells, and the variety of cells were against a diagnosis of Hodgkin's disease. The microscopic features were those of the destructive stage of eosinophilic granuloma of bone.

The patient was discharged from the hospital after receiving irradiation therapy. One 10-cm. circular anterior chest field was used. The physical factors were 220 kv., filter 0.5 mm. Cu plus 1.0 mm. Al; the HVL was 1.2 mm. Cu. The daily dose was 200 r and the total dose 1,600 r (air).

Another biopsy was performed on Feb. 11, 1944, two weeks after completion of the irradiation therapy. The microscopic picture was that of a less cellular and more fibrous lesion. Most of the specimen consisted of dense fibrous and in part hyalinized connective tissue, in which there were a moderate number of lymphocytes, large mononuclear and plasma cells. There were no eosinophils.

The patient returned for observation at the end of five weeks. At that time the mediastinal shadow had decreased in size from 7 to 6.4 cm.

First Recurrence: In May 1944, after being symptom-free for three months, the patient again noticed unusual malaise. At this time roentgenograms showed a mass along the left side of the sternum at the level of the aortic knob. This region was treated with high-voltage irradiation. A dose of 1,600 r (air) was administered to a 10 × 8-cm. anterior chest portal. The physical factors were the same as in the previous treatment. Improvement followed, and the patient was able to work for several months.

Second Recurrence: Anorexia was experienced in October 1944. The patient became weak and stated that she felt she "had the flu." She had a nonproductive cough and from October to December 1944 she lost 18 pounds. She was readmitted to the hospital at this time and was found to have an afternoon elevation of temperature (38° to 38.4° C.). Examination of the peripheral blood showed: 10,000 white cells (neutrophils 78 per cent, lymphocytes 13 per cent, monocytes 6 per cent, eosinophils 3 per cent), 5,800,000 red cells, and hemoglobin 60 per cent (Sahli). Chest films showed a marked increase in the size of the mediastinal mass (Fig. 9). It measured 12.4 cm. in width at the level of the aortic knob and 14 cm. in length. The area of bone destruction in the sternum persisted without evidence of healing. A second focus of bone destruction, 2 cm. in diameter, was observed in the lower half of the gladiolus. The left supraclavicular lymph nodes were only slightly, if at all, larger than on the original examination (December 1943). A large, firm, non-tender nodule, measuring 6 cm. in diameter, was present in the right axilla. This was removed on Jan. 24, 1945. It was an enlarged lymph node with an intact capsule and unusually soft, pale

yellow, friable tissue. Microscopic examination showed destruction of the architectural pattern in most regions. There were, however, a few recognizable lymph follicles with large secondary centers. The capsule was slightly increased in thickness. There were many foci of necrosis and moderate infiltration with neutrophilic leukocytes. Fibrosis and hyalinization were marked. Eosinophils and large mononuclear cells were also numerous and there were a few multinucleated giant cells (Fig. 8). Sections stained with Sudan IV showed many cells containing sudanotropic droplets. A diagnosis of eosinophilic granuloma of lymph node was made.

Additional irradiation was started on Jan. 27, 1945. Two 10 × 12-cm. anterior mediastinal fields were used, 300 r being given daily for seven days. The total dose was 2,100 r (air) to each field. The physical factors were 400 kv., 1.0 mm. Sn plus 0.25 mm. Cu plus 1.0 mm. Al filtration. The HVL of the beam of irradiation was 4.6 mm. Cu. The left supraclavicular lymph nodes were treated through a circular field, 7 cm. in diameter, 200 r daily for eight days, with the 220-kv. apparatus used for the first course of therapy given in January 1944. This extensive treatment resulted in severe prostration. The fever had disappeared by the time irradiation was completed.

During the next six weeks the patient gained 10 pounds in weight. Her appetite improved and she "felt fine" for the first time in eighteen months. Roentgenograms showed a decrease in the size of the mediastinal mass from 12.5 cm. in January 1945 to 7.5 cm. in March 1945.

Third Recurrence: The patient returned for examination in September 1945. During the preceding few months she had noticed moderate lassitude. There had been no recurrence of fever and no weight loss. The mediastinal mass was found to have increased in size. It measured 11 cm. at the level of the aortic knob (Fig. 10). Lateral views showed abnormal shadows extending from the anterior chest wall to the hila of the lungs. One of these shadows, also visible in the postero-anterior view, was thought to be an enlarged lymph node (Fig. 10).

Radiation was administered from the back through two portals (12 × 10 cm.) parallel to the vertebral column, directed obliquely toward the mediastinum. A dose of 2,000 r (air) was given to each portal during a period of ten days. A slightly enlarged left supraclavicular lymph node was treated with 900 r (air).

The patient was able to go to college and felt fairly well two months after this course of therapy. On Nov. 8, 1945, the mediastinal mass had a maximum measurement of 7 cm. Laminagrams of the sternum showed the lesion in the gladiolus to measure 3.5 × 2 cm., with some evidence of peripheral healing.

There was slight increase in the width of the mediastinal mass during the next two months, but no change occurred from January to March 1946. Mild symptoms of lassitude and weakness developed during this period but no treatment was given. The patient was able to attend college classes at this time (March 1946).

CASE 4: A white woman, aged 37 years, was admitted to University Hospitals on April 5, 1945, because of pain and swelling of the left thigh just proximal to the knee. The symptoms were first noted after she bumped her leg in January 1945. Subsequently she experienced periodic pain of increasing intensity on several occasions.

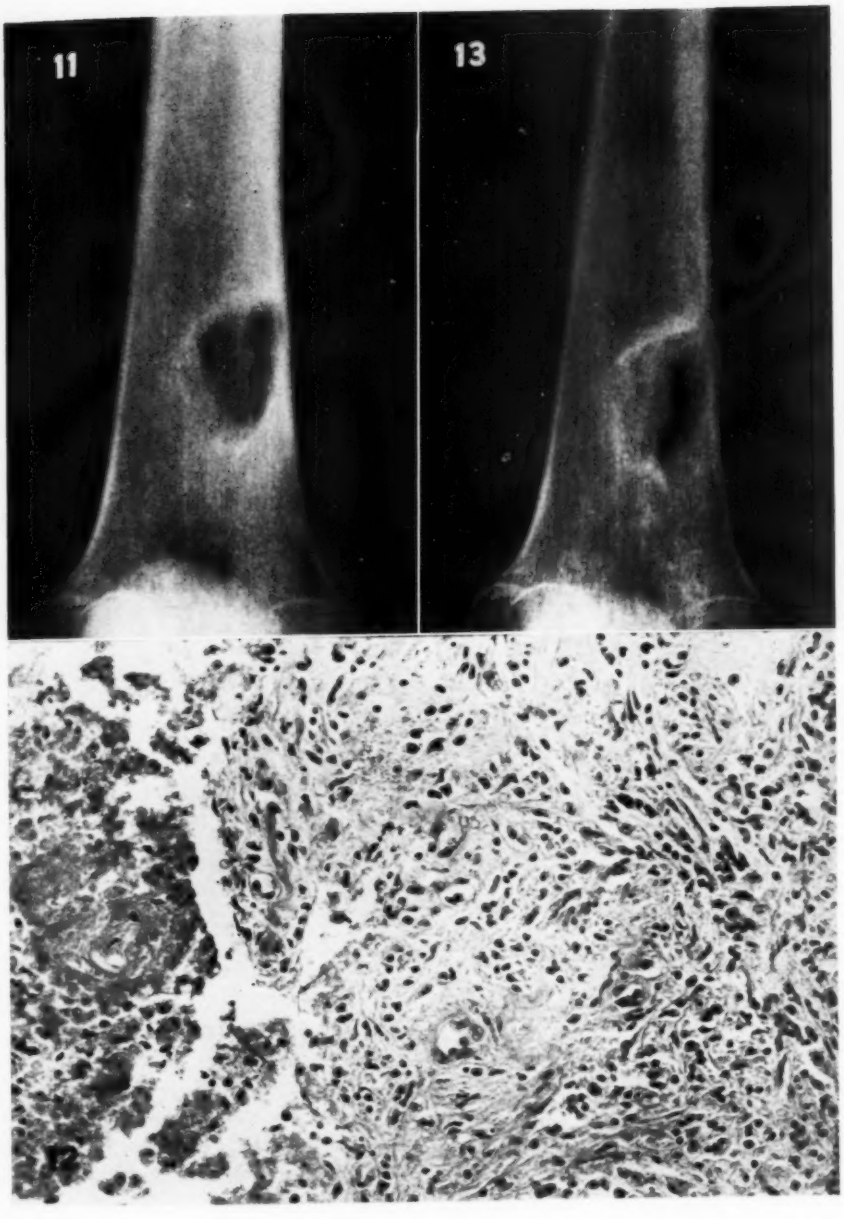
The patient was normally developed and nourished. Her temperature, at the time of hospitalization, was 37.3° C. There was slight tenderness on the anterolateral aspect and lower end of the left femur.

The Kline exclusion test was negative. The serum calcium, phosphorus, and alkaline phosphatase were all normal. The red cell count was 5,160,000; white cell count 7,350, with a normal differential count, with 1 per cent eosinophils. Roentgenograms showed an area of decreased density 6 cm. above the knee joint, in the anterolateral aspect of the left femur (Fig. 11). This lesion measured 3.5 × 2.5 cm. The margin of the defect was moderately sclerotic. The overlying periosteum was thickened, measuring 3 to 4 mm. The patient was operated on and a "smooth bulge," 4 cm. in length, was found on the medial aspect of the femur. The compact bone was hyperemic but firm. At this site the cortex of the bone was 3 mm. in thickness. In the adjacent bone was a cavity measuring 3.5 × 3.0 × 2.5 cm., in which there was soft friable reddish-brown material. The walls of the cavity were definitely sclerotic. The cavity was thoroughly curetted and swabbed with crude phenol and alcohol and lavaged with normal saline.

Microscopic examination revealed a richly cellular lesion with multiple small foci of necrosis. Fibroblasts and capillaries were numerous and there was moderate fibrosis. Eosinophils, lymphocytes, and large mononuclear cells were abundant (Fig. 12). This was considered to be the destructive stage of eosinophilic granuloma of bone.

Subsequent to treatment, serial roentgenograms have shown slow healing at the periphery of the lesion. In October 1945, five months after treatment, the lesion measured 3.0 × 2.5 cm. (Fig. 13).

CASE 5: A 4-year-old white boy first experienced "night pain" in his right leg in February 1945. He began to limp one month later. He was seen by a physician in April 1945, at which time a mass 3 × 4 cm. was present in the right iliac fossa. Roentgenograms showed an irregular area of bone destruction in the right ilium, measuring 4.5 × 3.5 cm. The borders of the defect were irregular in contour and it was not sharply defined (Fig. 14). The possibility of endothelial myeloma (Ewing) was suggested.



Figs. 11–13. Case 4.

Fig. 11. Anteroposterior view of the left femur made April 6, 1945, ten weeks after the first symptoms. The destructive lesion of the femur measures 3.5 × 2.5 × 2.0 cm. There is mild peripheral sclerosis. Periosteal reaction appears along the medial margin of the femur.

Fig. 12. Photomicrograph illustrating focal necrosis (on left), proliferated collagenous connective tissue with many lymphocytes and eosinophils. Hematoxylin and eosin. × 250.

Fig. 13. The lesion of the left femur shows peripheral healing five months after curettement and phenol cauterization. It measured 3 × 2.5 cm. on Oct. 26, 1945.

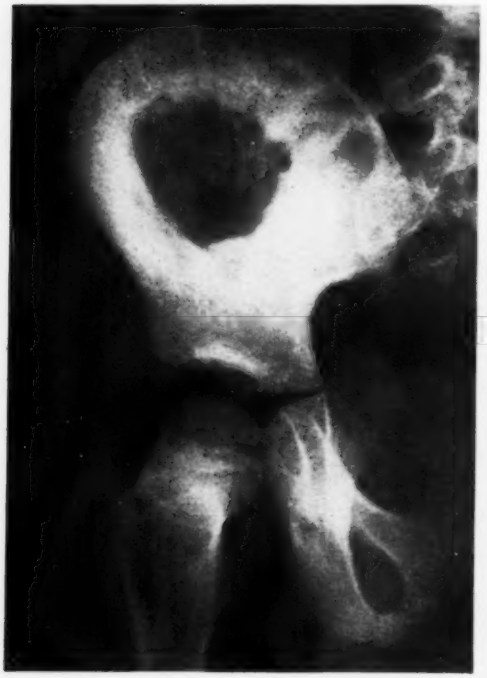


Fig. 14. Case 5. Oblique view of the right side of the pelvis made April 24, 1945, showing a destructive lesion 4.5 × 3.5 cm. The margin of the bone defect is irregular in outline and poorly defined in some areas.

The patient was admitted to Babies and Childrens Hospital in April 1945. His temperature on admission was 37.3° C. but rose to 40° C. or above each day. The white blood cell count was 10,400, with 1 per cent eosinophils.

A biopsy was done on May 1, 1945. Soft, friable, pinkish-yellow tissue was removed. Microscopic examination showed foci of necrosis, large mononuclear cells, abundance of eosinophils, and multinucleated giant cells which were considered to be characteristic of the destructive stage of eosinophilic granuloma of bone (Fig. 16).

The lesion was curetted on May 6, 1945. Serial roentgenograms have shown rapid healing. The osseous defect measured 2 × 1.5 cm. on Oct. 22, 1945 (Fig. 15).

SUMMARY

Forty-eight cases of eosinophilic granuloma of bone have been collected from the literature and analyzed. Five new cases are reported, making a total of 53 cases.

The sex of the patients was recorded in 43 instances; 36 were males and 7 were females. The age range was six months to fifty-eight years. Thirty-four of the patients were under twenty years of age and 20 were under ten years.

Nearly all bones proximal to the wrists and ankles were involved. Thirty-six patients had single lesions and in these the skull was involved in 36 per cent, and ribs and femurs in 16.6 per cent each. Ten patients had multiple lesions, with an average number of seven bones involved; in one case, reported by Farber, there were 25 lesions. In the group with multiple lesions, the ribs were involved in 33 per cent, vertebrae in 12.5 per cent, and the skull in 11 per cent.

A majority of the patients had mild to severe pain, swelling of the soft tissues, and tenderness over the site of the lesions, with a duration of a few days to several months. Some of the lesions were incidental findings at autopsy or on roentgenograms made for other purposes. A few patients had mild

Fig. 15. Case 5. The lesion of the right ilium has healed well five months after curettement. It measured 2 × 1.5 cm. on Oct. 22, 1945.

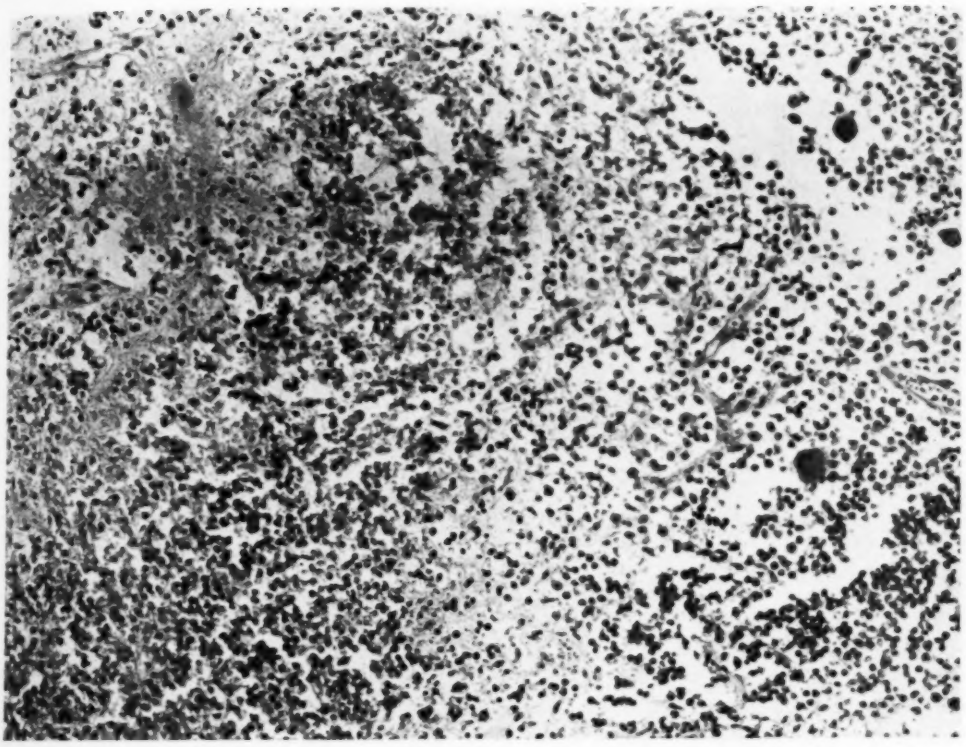


Fig. 16. Case 5. Photomicrograph of sections made from tissue removed from lesion of ilium. Numerous cells are present, including eosinophils, lymphocytes, and multinucleated giant cells. Necrosis is evident on the left. Hematoxylin and eosin. × *c.* 175.

systemic symptoms of fever, anorexia, lassitude, headache, and weight loss. Laboratory examination showed no abnormality other than slight leukocytosis and occasionally eosinophilia of 4 to 11 per cent. Roentgenographic examinations showed round, oval, or irregular areas of decreased density, usually 1 to 4 cm. in diameter. The lesions produced expansion of the bone in 5 cases and perforation of the cortex in at least 5 cases. Periostitis was observed in 14 cases and 3 lesions had sclerotic margins.

The early lesions appear cystic at gross examination, containing soft, friable, yellowish-brown and red material. A variety of cells, including large numbers of eosinophils, are seen on microscopic examination, but the characteristic cell is a large mononuclear cell with granular cytoplasm. The mononuclear cells have vacuolated cytoplasm in intermediate stages of the disease and their appearance has been considered as indicating a relationship between eosinophilic granuloma, Letterer-Siwe disease, and Schüller-Christian's disease. Jaffe and Lichtenstein have suggested that the three conditions may be due to an unknown infectious agent, eosinophilic granuloma being the most benign and localized form and limited to bone. Case 3 of the present series may represent a transition from eosinophilic granuloma to Letterer-Siwe disease, since there was lymph node involvement in addition to a lesion of the sternum.

Treatment by surgical excision, curettage, or irradiation has given good results in all previously reported cases. No death from the disease or attributable to the disease has been reported. Case 3 of the present series differs from others recorded

in the literature in that mild symptoms of lassitude persist twenty-eight months after the onset. A mediastinal mass also persists in this patient, although high-voltage radiation has been administered in doses which have relieved the symptoms and promoted healing of the bone lesions in other cases.

NOTE: Appreciation is extended to Dr. Maxwell Harbin and Dr. Frank Gibson for permission to include their cases in this report.

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The Osseous Manifestations of Eosinophilic Granuloma: Report of Nine Cases[1]

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THE EXISTENCE of a lesion in bone which histologically appears granulomatous, non-specific, and is infiltrated with histiocytes and eosinophilic leukocytes was first reported, simultaneously, in 1940, by Otani and Ehrlich (13) and by Lichtenstein and Jaffe (10). Undoubtedly the lesion had been seen previously, but its exact nature and course were not described. "Solitary granuloma of bone" was proposed by Otani and Ehrlich (13). Green and Farber (5) suggested " 'destructive granuloma of bone,' 'single' or 'multiple' as the case may be, adding parenthetically 'Hand - Schüller - Christian syndrome.' " Eosinophilic granuloma, as used by Jaffe and Lichtenstein (8), seems preferable and will be used in this paper.

Fig. 1. Case I. Solitary involvement of left frontal bone. The lesion is oval and appears to have originated in the diploe, with extension through both the inner and outer tables.

Since 1940, a number of authors have reported single examples or small groups of cases, leading to considerable discussion of the relationship of this lesion to the older entities of Hand-Schüller-Christian's disease, or lipogranulomatosis, and Letterer-Siwe's disease, also called reticulosis or non-lipoid histiocytosis (Jaffe and Lichtenstein, 8; Green and Farber, 5; Mallory, 11). Disagreement concerning the exact terminology is, therefore, to be expected.

It is our purpose to present the roentgen findings in 9 cases, confirmed by biopsy, which were seen in an Army General Hospital, together with the pertinent clinical and laboratory findings. In each case the biopsy sections were reviewed and the histopathologic diagnosis confirmed by the Army Medical Museum.

CASE I (Fig. 1): White male, 21 years of age. Onset September 1943 with constant headaches and pain in the orbits. There were no convulsions,

[1] Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

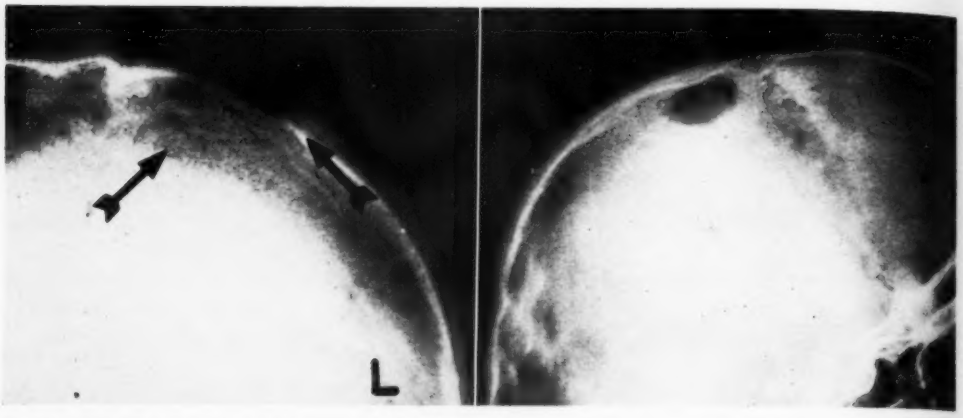

Fig. 2. Case II. Left parietal bone. The lesion is well circumscribed, but the edges are slightly irregular.

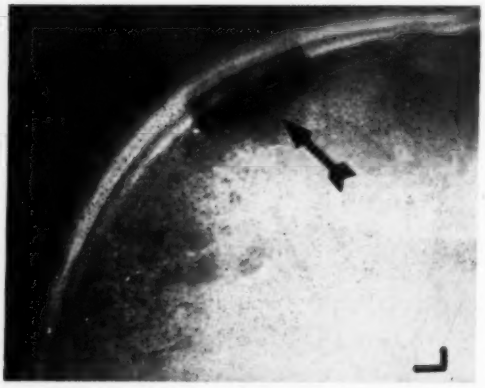

Fig. 3. Case III. Left parietal bone. The lesion is oval and well circumscribed. At operation several small avascular fragments of bone were found, but these could not be seen on the roentgenogram.

vomiting, or visual changes. In October, a fluctuant, tender, but non-pulsating mass developed in the left forehead. A roentgenologic bone survey revealed a solitary lesion in the left frontal bone; no similar lesions were present in other bones.

Laboratory Findings: The Kahn test was negative. Nothing unusual was found on urinalysis, which was negative for Bence-Jones protein. The white blood count was 5,700 (66 per cent polymorphonuclears, 5 per cent eosinophils); blood serum calcium 10 mg. per 100 c.c.; phosphorus 3.5 mg. per 100 c.c.; total protein 6.1 gm. per 100 c.c., basal metabolic rate + 7; blood cholesterol 194 mg. per 100 c.c.

Although at biopsy in November the tumor appeared grossly malignant, involving both tables of the skull, the histologic picture was the classical one of eosinophilic granuloma.

CASE II (Fig. 2): White male, 24 years of age. Onset October 1943 with trembling and numbness of right hand. The patient had two episodes of unconsciousness but no headaches. A small mass was palpable in the left parietal region. Physical examination showed the right arm to be weaker than the left. Except for the left parietal lesion, a roentgenographic bone survey was negative.

Laboratory Findings: The Kahn test was negative. White blood counts of 5,600 to 8,000 were obtained, with 50 to 60 per cent polymorphonuclears, and 3 to 5 per cent eosinophils. The sedimentation rate was normal; total serum protein 7.1 gm. per 100 c.c.; albumin-globulin ratio 1.3 to 1; blood cholesterol 133 mg. per 100 c.c.; serum calcium 11.0 mg. per 100 c.c.; phosphorus 4.0 mg. per 100 c.c.; alkaline phosphatase 4.9 Bodansky units.

At operation a mass of soft friable tissue measuring about 3 × 4 cm. was removed. This involved both tables of the skull and had invaded the dura and cortex.

Histologically the lesion was an eosinophilic granuloma.

CASE III (Fig. 3): White male, 27 years of age. One month following an accident in which the patient was struck on the top of his head by the turret of a tank and knocked unconscious momentarily (with persistent headache for four days thereafter), a small mass, soft and semi-fluctuant, developed in the occipitoparietal region. The patient was admitted to this Army General Hospital about four and one-half months after the accident. In addition to the headaches, symptoms had included blurring of vision, mainly in the left eye, episodes of dizziness, and occasional tinnitus in the left ear. On roentgenographic examination, a lesion was seen in the left occipitoparietal region. A bone survey failed to reveal other lesions.

Physical examination revealed a soft, semi-fluctuant tumor about 3 cm. in diameter in the scalp in the left occipitoparietal area. The pupils reacted poorly to light, but the eyes were otherwise normal.

Fig. 4. Case IV. Right parietal bone. Involvement of the outer table is more marked. Although a small soft-tissue mass is frequently found at the site of these lesions, there was in this case a palpable defect.

Laboratory Findings: The Kahn test was negative. Nothing unusual was found on urinalysis. The red blood count was 5,400,000; hemoglobin 107 per cent; white blood counts 9,000 to 13,200 (63–71 per cent polymorphonuclears, 31–30 per cent lymphocytes, 2–2 per cent monocytes, 3–6 per cent eosinophils, 1 per cent basophils); blood non-protein nitrogen 26 gm. per 100 c.c.; blood sugar 73 mg. per 100 c.c.; blood cholesterol 154 mg. per 100 c.c.; serum phosphorus 3.5 mg. per 100 c.c.; alkaline phosphatase 4.9 Bodansky units.

At operation the surgeon found sequestrated bone fragments with an old organized clot. Following curettage, the pathologist reported that the lesion was eosinophilic granuloma of the bone.

CASE IV (Fig. 4): White male, age 19 years. Onset three weeks before admission, with frontal headaches associated with diplopia and dizziness. There was a spot over the vertex which was tender to pressure, and palpation revealed a probable bone defect at this point. Except for the lesion in the right parietal bone, a roentgenographic survey failed to reveal any bone involvement.

Laboratory Findings: The Kahn test was negative. Urinalysis was normal. The white blood count ranged from 5,800 to 9,800. Differential cell counts were repeatedly within normal limits except that on one occasion there were 7 per cent eosinophils. Hemoglobin determinations were normal; blood cholesterol 132–167 mg. per 100 c.c.; blood calcium 11 mg. per 100 c.c.; phosphatase 4.2 Bodansky units.

Biopsy showed eosinophilic granuloma.

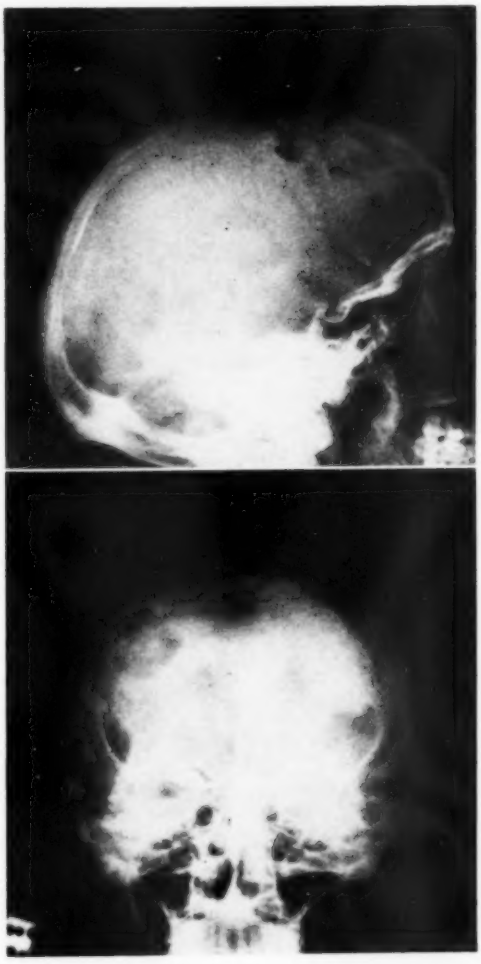

Fig. 5. Case V. Skull. There is extensive involvement of the frontal bone and the anterior superior portions of both parietal bones. The appearance suggests that there has been a coalescence of several smaller lesions. Syphilitic osteomyelitis is simulated, but involvement appears to be greater in the outer table, and the lesion extends across the suture line.

CASE V (Figs. 5 and 6): White male, age 26 years. The chief complaint was of a mass in the right frontal area of the scalp which had gradually increased in size, with occasional periods of slight recession. There were constant pain and tenderness in the affected area.

Laboratory Findings: The Kahn test was negative. Nothing abnormal was found on urinalysis,

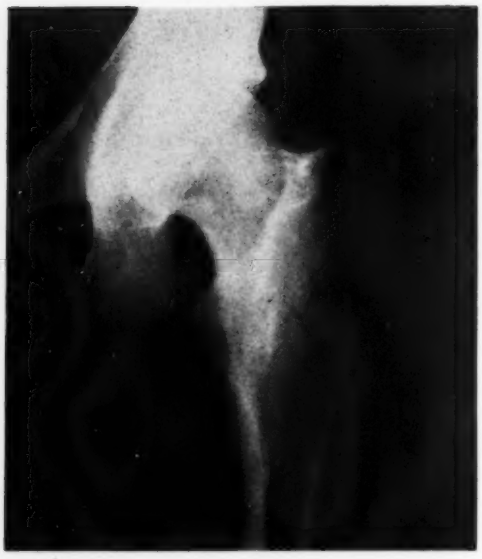

Fig. 6. Case V. Left femur. This intertrochanteric lesion was asymptomatic and was brought to light only on a skeletal survey. It is confined to the medullary portion of the shaft and is surrounded by a thin zone of sclerosis. A similar lesion was found in the right humerus.

which was negative for Bence-Jones protein. The sedimentation rate was 16 mm./hr.; serum calcium 10.7 mg. per 100 c.c.; phosphorus 3.8 mg. per 100 c.c.; alkaline phosphatase 5.1 Bodansky units; acid phosphatase 2.9 Bodansky units; blood protein 6.7 gm. per 100 c.c.; albumin-globulin ratio 4.7 to 2. The complete blood count was within normal limits.

Roentgenologically, there is seen to be a large irregularly shaped defect involving almost the entire frontal bone and the anterior superior portions of both parietal bones (Fig. 5). The defect appears to be due to the coalescence of several smaller lesions. Both tables of the skull are involved, and the suture line is crossed. The possibility of syphilitic osteomyelitis was considered in this patient. An oval osteolytic lesion was also found in the intertrochanteric region of the left femur (Fig. 6). There was also a small oval osteolytic lesion, 1.5 cm. in diameter, in the proximal end of the shaft of the right humerus. The lesions in the femur and humerus were asymptomatic.

Biopsy showed eosinophilic granuloma.

CASE VI (Figs. 7 and 8): White male, age 32 years. In January 1944, the patient first began having pain in the region of the right hip, aggravated by walking. He was then transferred to a hospital, where the only positive finding was a cyst-like lesion in the mandible, which was without symptoms. This was removed by the dentist. Unfortunately, a report of the pathologic study of this tissue is not available. Following hospitalization and symptomatic treatment for arthritis, the patient was placed on limited service.

In June 1944, the patient began to suffer from pains in the occipital region of the skull and in the right shoulder. In August 1944, a biopsy showed the lesion in the shoulder to be an eosinophilic granuloma. A course of roentgen therapy relieved the symptoms but, following a convalescent furlough, similar pain developed in the left shoulder. The patient was then referred to this General Hospital for further deep roentgen therapy. Except for the roentgenographic findings, clinical studies revealed nothing of significance.

Laboratory Findings: The Kahn test was negative. The red blood count was 5,250,000; white blood count 9,600, with 69 per cent segmented cells and 23 per cent lymphocytes; total blood serum protein 8 gm. per 100 c.c.; albumin-globulin ratio 5.2 to 2.9; blood calcium 11 mg. per 100 c.c.

Roentgenograms revealed an irregular defect in the left occipital bone (Fig. 7). There was an area of destruction in the mid-portion of the right scapula. The left scapula appeared normal. The pelvis showed several rounded areas of diminished density in the right ischium (Fig. 8). A review of the films from the previous hospital showed regression of the lesions in the right scapula and pelvis. No change was noted, however, in the granuloma in the occipital bone, and following additional therapy roentgenograms failed to show any appreciable change.

CASE VII (Figs. 9 and 10): White male, age 19 years. In September 1944, the patient experienced a severe attack of pain in the right thigh, which lasted for fifteen or twenty minutes. The pain recurred a few days later but was only transient. He had no further trouble during the next few months except that, on alighting from a bus or making a similar movement, there would again be sharp pain in the right thigh. In February 1945, while riding on a bus, he experienced an aching pain on the right, involving the whole area from hip to knee, which persisted until his admission to this Army General Hospital in June 1945. The pain was made worse by weight-bearing and, although greatly alleviated by rest, was severe at night, interfering with his sleep. Later, motion of the right hip became restricted. In February and March 1945, there was a loss of 30 pounds in weight associated with anorexia. The history was otherwise noncontributory.

Roentgenograms revealed a soft-tissue mass in the left perihilar region and an osteolytic lesion in the right femur. The patient was transferred to this Army General Hospital for deep roentgen therapy.

Laboratory Findings: The Kahn test was negative, and there were no abnormal findings on urinalysis. The red blood count was 4,450,000; hemoglobin

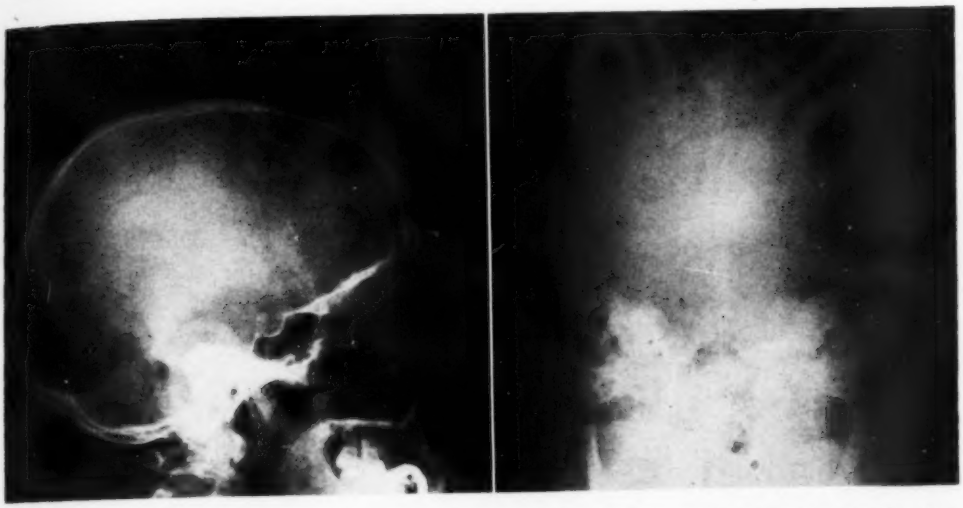

Fig. 7. Case VI. Skull. The lesion involves the left occipital and parietal bones. It is irregular, but the edges are rounded, suggesting a coalescence of several smaller lesions. There is a so-called "geographic" appearance.

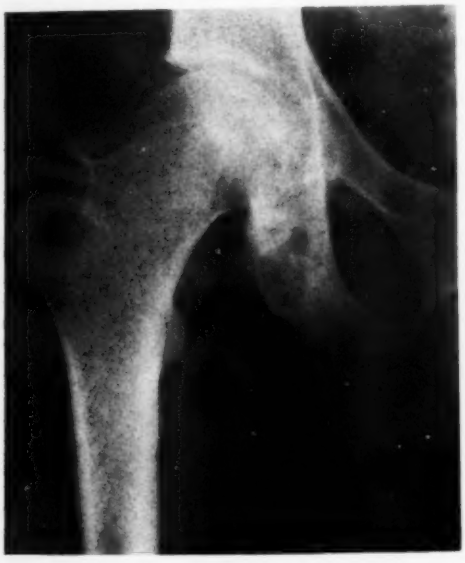

Fig. 8. Case VI. Right hip, showing a group of small, oval osteolytic lesions in the ischium. Following roentgen therapy, these areas partially filled in with new bone. Roentgen evidence of bone regeneration following irradiation was not our usual experience.

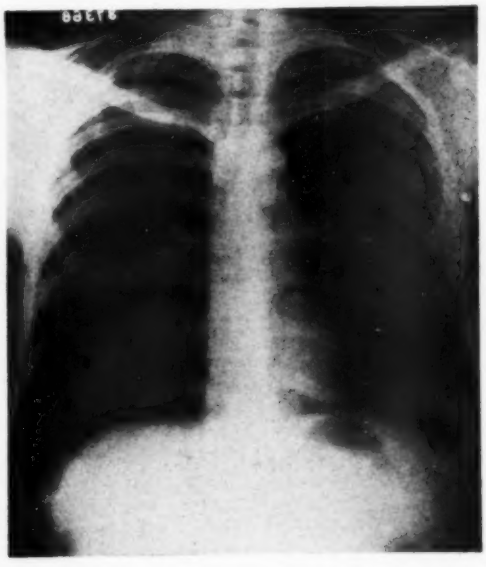

Fig. 9. Case VII. Chest. A small but definite soft-tissue tumor is seen in the left perihilar region. It is believed to be a lymph node. It underwent partial regression during the period of observation in the hospital. The exact nature of this mass was not determined.

85 per cent; white blood count 12,800, with 76 per cent polymorphonuclears, 19 per cent lymphocytes, 5 per cent eosinophils; sedimentation rate 38 mm./hr. (corrected); basal metabolic rate −26; blood serum protein 6.5 gm. per 100 c.c.; albumin-globulin ratio 3.9 to 2.6; blood serum calcium 11.1 mg. per 100 c.c.; phosphorus 3.0 mg. per 100 c.c.; phosphatase 7.0 Bodansky units. Additional complete blood counts revealed eosinophils in the following percentages, 0, 6, 5, 5; the white blood counts remained slightly increased. The heterophile agglutination was 1–28. The Lederle tuberculin patch test was 2 plus at the 96-hour reading.

Biopsy revealed an eosinophilic granuloma of the

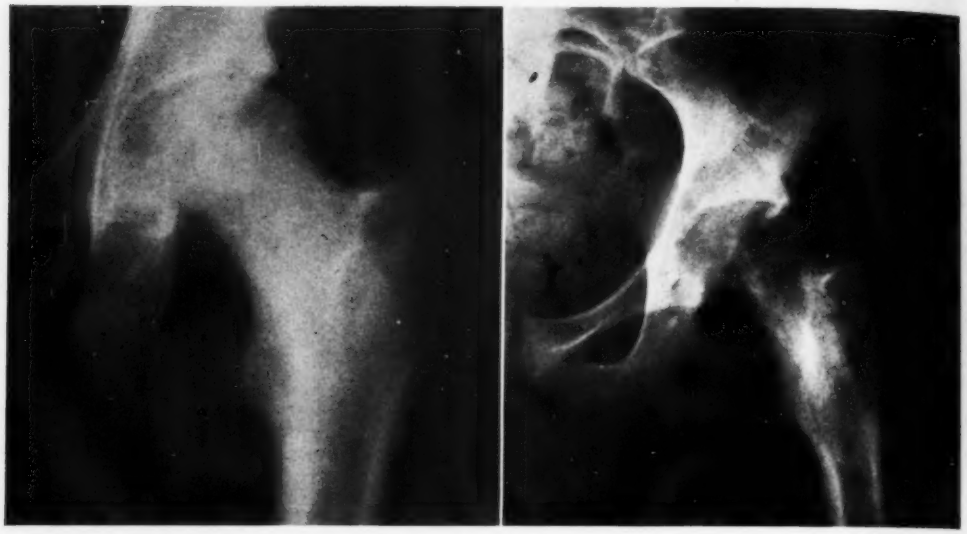

Fig. 10. Case VII. Right femur, showing osteolytic involvement of the subcapitate region. This gave rise to severe pain. Roentgen therapy relieved the pain, but the lesion nevertheless increased in size, as shown in the view on the right.

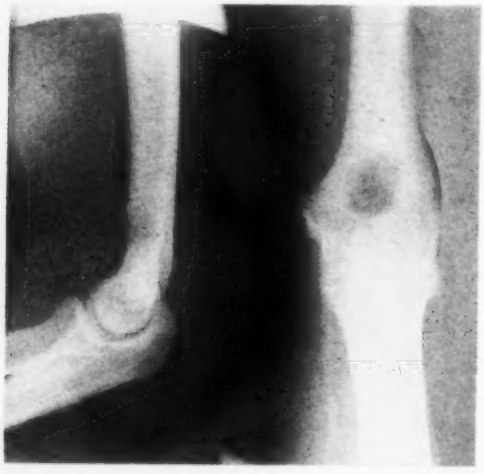

Fig. 11. Case VIII. Right humerus. The oval, osteolytic lesion in the intercondylar area apparently originated in the medullary portion of the bone with erosion of the cortex on the anterior aspect. There is also a small amount of subperiosteal new bone formation in this area.

femur. Roentgenograms showed that the tumor in the left perihilar region, believed to be an enlarged lymph node, had decreased considerably in size since March.

Following deep roentgen ray irradiation, for a dose of 1,800 r, the patient was entirely relieved of pain and desired to be up and about. A roentgenogram of the hip, however, taken shortly after the termination of therapy, showed an increase in size of the osseous lesion.

Subsequent to this, a small lymph node was palpated in the left supraclavicular region. In an effort to discover the nature of the process in the lung, this node was biopsied, but microscopic examination showed only fibrosis of undetermined etiology.

CASE VIII (Fig. 11): White male, age 25 years. In January 1945, the patient experienced intermittent pains in his right shoulder, associated with motion. These became more severe and gradually extended down the arm. Three weeks after onset, a swelling of the right elbow was first noticed. Following unsuccessful symptomatic treatment, a roentgenogram was taken which showed a punched-out area in the distal end of the shaft of the right humerus, and the patient was sent to an Army General Hospital for treatment. Except for the lesion in the humerus, a bone survey failed to reveal any evidence of disease.

Laboratory Findings: The Kahn test was negative. The red blood count was 5,300,000; hemoglobin 100 per cent; white blood count 7,500, with 62 per cent neutrophils, 32 per cent lymphocytes, 6 per cent eosinophils; sedimentation rate 3 mm./hr. Other laboratory studies were non-contributory.

The lesion was curetted, and the biopsy report was eosinophilic granuloma.

CASE IX (Figs. 12 and 13): White male, age 21 years. In April 1944, the patient had two lower incisors extracted because they were loose in their sockets. Following this, the sockets never seemed

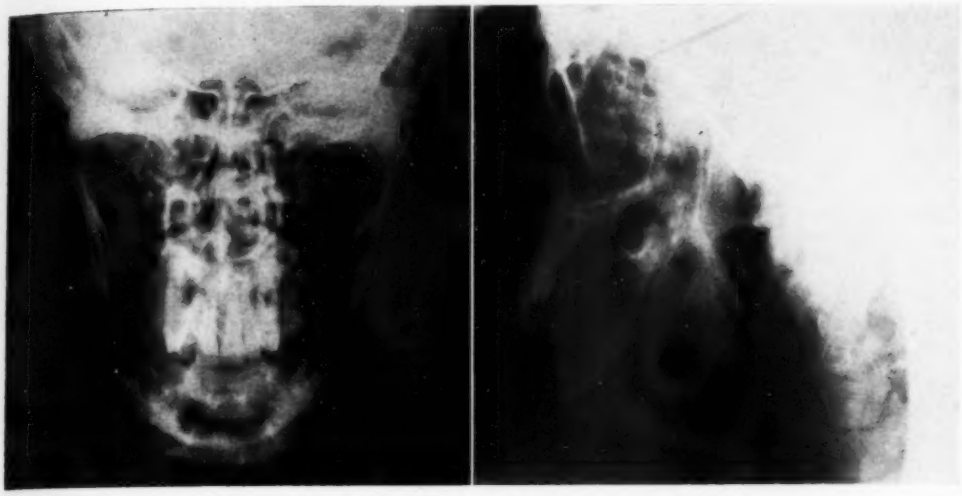

Fig. 12. Case IX. Mandible. Multiple cystic lesions present in the mandible on both sides caused this patient to seek medical attention for an initial complaint of looseness of the teeth.

to heal, and the patient was aware that other lower teeth were loose. For several months this was thought to be due to pyorrhea. In December 1944, at a routine dental check-up, a cyst of the mandible was found, following which the rest of the lower teeth were removed, and a biopsy was taken. Early in February 1945, the patient complained of pain in both thighs. The pain was intermittent and present only during inclement weather. The patient was admitted to an Army General Hospital on May 14, 1945.

Roentgenologically there were numerous osteolytic lesions involving the skull. These had smooth edges and were surrounded by a fine zone of sclerotic bone. Similar lesions were present in the right clavicle and the mid-third of the shaft of each radius. There was severe involvement of the lower halves of both femora roentgenologically simulating fibrous dysplasia or osteitis fibrosa cystica. There were, in addition, numerous destructive cyst-like lesions of the mandible.

While roentgen therapy was being administered to the lesions mentioned above, numerous small osteolytic lesions appeared in the proximal halves of the shafts of the tibiae. Pain in the thighs was relieved during a course of roentgen therapy, although no roentgenologically demonstrable regression of any of the lesions was observed.

Laboratory Findings: The Kahn test was negative. Red blood counts were 4,030,000–4,500,000; hemoglobin 79 per cent. Differential counts showed 69–66 per cent neutrophils; 27–32 per cent lymphocytes, 2–1 per cent monocytes, 1–1 per cent eosinophils, 1 per cent basophils. Blood serum calcium was 9.6 mg. per 100 c.c.; phosphorus 3.8 mg. per 100 c.c.; alkaline phosphatase 7.9 Bodansky units; sedimentation rate slightly increased; blood uric acid 2.6 mg. per 100 c.c.; blood cholesterol 170 mg. per 100 c.c. Smears obtained from the sternal marrow showed a normal picture.

Biopsy from the mandibular cyst and the right clavicle revealed eosinophilic granuloma.

DISCUSSION

Due probably to the fact that most of our patients are drawn from military personnel, all 9 are young, white, adult males, ranging in age from nineteen to thirty-two years. This is of interest in that the group is older than many series previously reported. One case, reported by Green and Farber (5), was that of a child of two years; Otani and Ehrlich (13) found the condition in a patient of 35 years, and Versiani and his associates (17) had a patient 50 years of age. These, we believe, represent the extreme age range reported to date. In 24 cases which we have found in the literature, in addition to the 9 here reported, the majority of the lesions were seen in the first three decades of life.

Nine of the 10 cases reported by Green and Farber (5) were in males; of the remaining cases in which the sex was given, 11 were in males and 4 in females. In our series all the patients were males. This predominance of males seems to be of

questionable significance since only a small number of cases have been reported, and the present series at least was gathered in a fixed Army General Hospital.

No definite racial or geographical distribution could be discovered, either on reviewing the cases in the literature or from our own group. Nor was any familial tendency observed.

Clinical Findings: The symptoms associated with eosinophilic granuloma usually depend upon the location and extent of involvement of the affected bones. Green and Farber (5) noted in their series that pain was usually the presenting symptom when bones other than the skull were involved. Seven of our 9 patients (Cases I, IV, V, VI, VII, VIII, and IX) suffered from pain localized in or about the site of a bone lesion. In most patients, the pain was from slightly to moderately severe; in 2 (Cases VI and VII) it was very severe. Severe pain was also the complaint in a case reported by Kernwein and Queen (9). The pain is usually aggravated by motion, weight-bearing, or palpation.

Since in most instances the pain is not of great severity, several weeks or even months may elapse before the patient is seen by a physician. One case has been reported in which pain was present for two years (2) before discovery of the lesion. In Cases V and IX, there were silent osseous lesions which were discovered only on a skeletal survey, indicating that the disease may exist for some time before symptoms develop.

When the lesion is localized in a flat bone, as the skull or ribs, the presenting symptom is likely to be a tender swelling, as in some of the reported cases (1, 3, 4, 6) and in our own Cases I, II, and III. One exception was noted in Case IV of our series, in which a tender palpable defect was found over the vertex of the skull. Even when the skull is extensively involved, the neurological signs are likely to be minimal. Headache has been a frequent complaint in our own and in reported cases, but the term "headache" is subject to wide interpretation; it may be due to pain at the site of the lesion in the skull. In Case II, in which the lesion was located over the left parietal cortex, there were tremor and numbness of the right hand and there had been two episodes of unconsciousness. In Case IV, diplopia and dizziness were present, secondary to a lesion in the right parietal bone. Two cases of skull involvement have been reported in which there was a Bell's palsy: in one, reported by Osborne, Freis, and Levin (12), there was roentgen evidence of temporal bone involvement; in the other, one of the "Cabot cases" (3), an involvement of this bone was not demonstrated, although the presence of a small lesion strategically located was suggested by Dr. Green in discussing the case.

A rare initial symptom, present in our Case IX, is looseness of the lower teeth; subsequent roentgen-ray examination disclosed the destructive process in the mandible. In a case with primary involvement of the mandible reported by Thoma (16), a painful swelling of the jaw was found with malposition of the teeth, but no mention was made of their being loose. Another patient (Case VI) had a cyst in the mandible, but this was asymptomatic and no pathologic study was available.

Although in some of our patients lesions in the long bones were present, and these men had been exposed to the rigors of military life, in no instance was a pathological fracture found. In only one case has a fracture been reported in the literature, and this was found at biopsy (Otani and Ehrlich, 13).

In none of our cases was there any noteworthy change in pulse or respiration, nor was intermittent or sustained elevation of temperature found. Only one of our patients (Case VII) reported a weight loss, 30 pounds within two months. A similar finding was reported by Kernwein and Queen (9), one of their patients having lost 25 pounds in weight.

No proved visceral manifestations of eosinophilic granuloma seem to have been found. If, as has been suggested, this disease is related to Hand-Schüller-Chris-

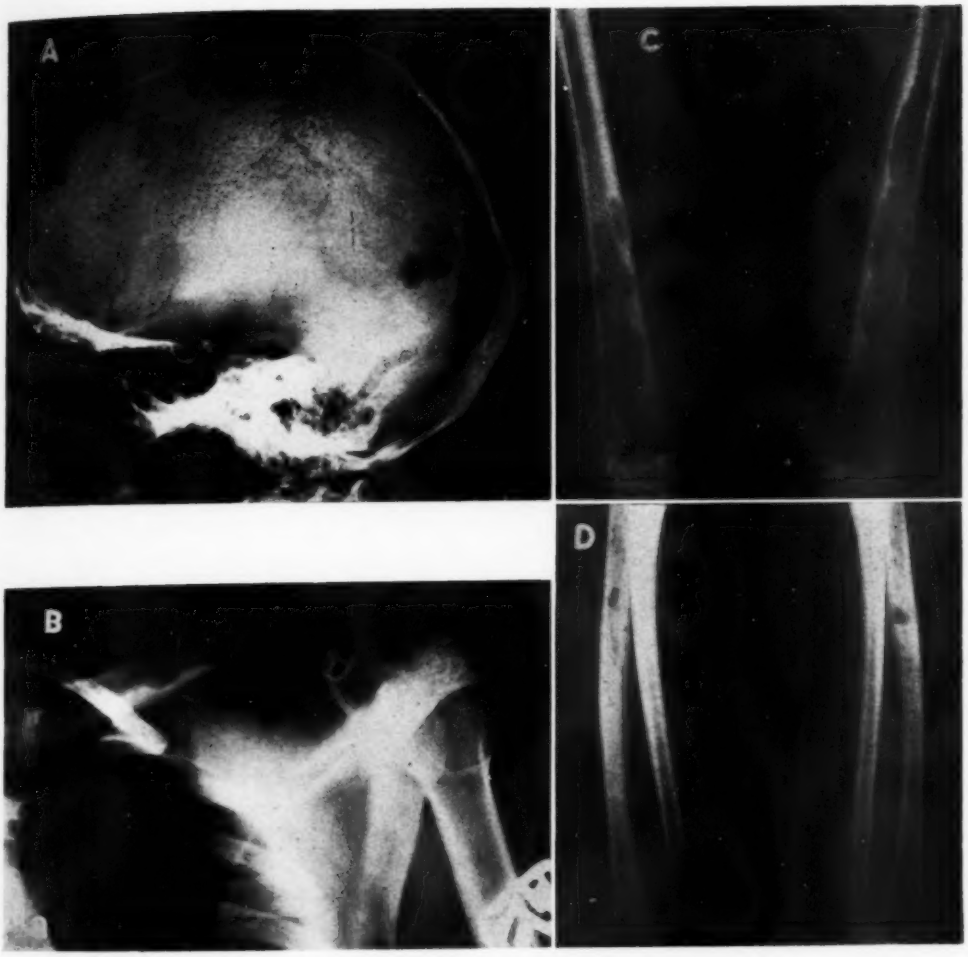

Fig. 13. Case IX. A. The skull. B. Right clavicle. C. Both femora. D. Both radii. A multiplicity of lesions was present in this patient. Very few of the lesions were symptomatic, most of them being brought to light only on a skeletal survey. The alkaline phosphatase level was 7.9 Bodansky units.

tian's disease (Green and Farber, 5; Jaffe and Lichtenstein, 8; and Mallory, 11), other organs, particularly those of the reticulo-endothelial system, might be expected to show lesions of the same type. In our series, we were unable to find any evidence of enlargement of the liver, spleen, or lymph nodes, except in one patient (Case VII) in whom an enlarged lymph node was found in the left perihilar region, and a palpable node was found in the left supraclavicular area. Biopsy of the node from the supraclavicular region, however, showed only a fibrotic process. The lymph node present in the left hilum (Fig. 9) regressed while the patient was under hospital observation. No statement as to its exact nature can be made.

Two cases of eosinophilic granuloma associated with diabetes insipidus have been reported by Versiani *et al.* (17) and by Thoma (16). This is an interesting observation, since diabetes insipidus is described as part of the Schüller-Christian triad. There was no definite roentgen evidence of involvement of the base of the skull in

either case and, since there were no pathological studies of the tissues in and about the pituitary, the cause was not established microscopically.

Laboratory Studies: No marked deviation from the normal in the blood count was found in any of our patients. A slight leukocytosis was present in only 2 (Cases VII and IX) but has been reported by others (Jaffe and Lichtenstein, 8; Green and Farber, 5). A number of authors have found an increase in the percentage of eosinophils in the peripheral blood (Lichtenstein and Jaffe, 10; Bass, 1; Horwitz, 7). The percentage of eosinophils in the differential cell counts of our patients is given in the case reports. In 6 of the cases, at one time or another, the eosinophil count exceeded 4 per cent; the highest count was 7 per cent. A slight increase in the percentage of eosinophils, therefore, while not a constant finding, may suggest that a bone lesion is an eosinophilic granuloma. A sternal marrow puncture performed in Case IX produced a normal smear.

No deviations from the normal were found in blood serum calcium and phosphorus studies. The proteins of blood plasma and the albumin-globulin ratio were consistently within normal limits. In only 2 of the cases was the alkaline phosphatase increased: in Case VII, 7 Bodansky units, and in Case IX, 7.9 Bodansky units were reported. The former patient had a solitary osteolytic lesion; the latter, multiple osteolytic lesions. Blood cholesterol ranged from 132 to 194 mg. per 100 c.c., and in only one case exceeded 170 mg. A serologic test for syphilis was negative in all cases. The sedimentation rate was elevated in 3 cases, in 2 of which the deviation from normal was slight. Other serologic and chemical determinations were within normal limits. Several authors (Jaffe and Lichtenstein, 8; Otani and Ehrlich, 13; Green and Farber, 5) have made smears and cultures of the lesions, but no pathogenic organisms have been discovered.

Roentgenographic Appearance: The osseous lesions reported in this study have all been osteolytic and tend to be rounded (Figs. 1, 2, 3). The shape, however, may be variable, suggesting the coalescence of several smaller lesions, and in the cranial vault giving rise to a "geographic" appearance (Figs. 5 and 7). The lesions are usually sharply defined (Fig. 2). A very thin zone of sclerosis may surround the osteolytic area but usually does not. Aside from this, there is very little evidence of reactive new bone formation. In the skull, the lesion has little respect for the suture lines and usually involves both tables of the calvarium (Fig. 5). When involvement of the outer table is greater, there is usually a soft-tissue mass, which is often palpable. In the long bones, the lesion has been seen to erode through the cortex (Fig. 11), but this is not a frequent occurrence. Very little subperiosteal new bone formation has been noted. It is felt that these factors attest to the benign and insidious growth of the granulomas.

Practically every bone in the body, with the exception of the carpals, metacarpals, and phalanges, and the corresponding bones of the feet, have been found to harbor eosinophilic granuloma. There seems to be no characteristic localization of the lesion within the bone; the epiphysis, metaphysis, and the diaphysis are all known to have been involved. In Cases I, II, III, IV, and VIII, the lesion is assumed to be solitary, since no additional lesions could be demonstrated by a skeletal survey. The remaining patients showed multiple bone involvement, and in several instances there were multiple lesions in individual bones.

Differential Diagnosis: On the basis of the roentgen appearance, the diagnosis of eosinophilic granuloma may be strongly suggested, but histopathologic confirmation is necessary. A well circumscribed osteolytic lesion, with little evidence of reactive new bone formation, in a child or young adult, is suggestive of a granuloma. Solitary cyst-like lesions in the cranial vault, about 1 to 1.5 cm. in diameter, in young adults are, in our experience, often

eosinophilic granulomas (Figs. 1, 2, 3, 4). The condition may, however, be closely simulated by a fibrosing osteitis developing after a closed injury to the skull. Meningiomas eroding the cranial vault and epidermoid cysts can usually be differentiated from eosinophilic granulomas on an analysis of the films. The meningiomas erode the inner tables more than the outer, and the epidermoid cysts originate in the diploe and expand through both the inner and outer tables of the cranial vault.

The various osseous lesions encountered in this series roentgenologically closely simulated a variety of pathological entities. The similarity to the osseous lesions of Hand-Schüller-Christian's disease is well illustrated in Figures 7 and 13. The likeness to cystic lesions of bone, including those of the jaw (Fig. 12), solitary bone cysts, osteitis fibrosa cystica, and fibrous as well as chondrodysplasia of bone, is apparent in Figures 8 and 13, C and D. In one patient, a low-grade osteomyelitis, probably syphilitic, was considered when the skull films (Fig. 5) were first examined. Figure 10 shows a lesion which radiographically closely simulates a metastatic tumor. Figure 11 is suggestive of an osteogenic sarcoma.

This is obviously not a complete list of the lesions which may be simulated radiologically. Ewing's tumors, myelomas, giant-cell tumors, and other osseous lesions which may be confused have been mentioned by others. One of the patients in this series was transferred to this hospital with a tentative diagnosis of multiple myeloma.

A roentgenographic bone survey is usually necessary to find multiple lesions, many of which are apt to be asymptomatic.

Treatment: Treatment is either by surgery or roentgen therapy, or a combination of the two, or by watchful waiting. Jaffe and Lichtenstein (8) have reported spontaneous healing of an otherwise untreated lesion. Operation on at least one lesion found in a patient is obviously necessary for confirmation of the diagnosis. Curettage of a small lesion is apparently adequate treatment, and uneventful healing usually follows. We were unable to determine whether or not roentgen therapy was helpful in combination with curettage.

TABLE I: TREATMENT IN NINE CASES OF EOSINOPHILIC GRANULOMA OF BONE

Case	Treatment	Total Roentgen Irradiation to Any One Site
I.	Biopsy	None
II.	Surgical and roentgen therapy	2200 r
III.	Surgical	None
IV.	Biopsy	None
V.	Biopsy and roentgen therapy	1500 r × 2
VI.	Surgery and roentgen therapy	1200–1200–600 r
VII.	Biopsy and roentgen therapy	1800 r
VIII.	Surgical	450–1200 r.
IX.	Biopsy and roentgen therapy	1200 r × 9

Roentgen therapy was administered with the G. E. Maximar 220-kv. machine. The factors were: 220 kv., 15 ma., 0.5 to 1.0 mm. Cu plus 1.0 mm. Al filter, HVL. 0.9–1.35 Cu, 50 cm. t.s.d. Dosages varied from 150 r every other day to three times a week, and 200 r every day to every other day. The portals were of adequate size to cover the individual lesions or involved areas.

Following irradiation pain was relieved. In this series, with a relatively short period of follow-up, there was no roentgen evidence that such therapy altered the course of the disease, except possibly in Case VI, in which there was evidence of regression subsequent to treatment. This, of course, may have been coincidental. In Case IX, while the patient was receiving a course of roentgen therapy, new lesions appeared. Since we were unable to follow these patients over a long period of time, it is possible that delayed resolution with reossification may have taken place subsequently in some instances.

Cases II, V, VI, VII, and IX of this series received roentgen therapy by several technics, varying from small and infrequent to large and more frequent doses (see Table I). The results were comparatively uniform. Pain was relieved and, when function of an extremity had been limited, it was resumed. Such relief continued during the period of our observation. Subsequent roentgenographic studies did not show a greater or earlier degree of bone repair in the irradiated areas as compared

with those areas which had received no irradiation. In Case VII, there was an increase in the size of the granuloma, even though treatment had involved biopsy and roentgen irradiation.

In our experience, roentgen therapy is indicated for the relief of pain. It is also possible that small doses of roentgen rays over longer periods might be helpful in obtaining radiographically demonstrable regression of many of these lesions.

SUMMARY

1. Nine cases of eosinophilic granuloma of bone, confirmed by histopathological examination at the Army Medical Museum, have been reported, with clinical and laboratory findings.

2. The roentgenographic manifestations and the differential diagnosis have been discussed.

3. In one patient, there was an enlarged perihilar lymph node of undetermined etiology which underwent partial spontaneous regression during the limited period of observation.

4. The necessity for confirmation of the diagnosis by biopsy has been stressed.

5. The use of roentgen therapy has been discussed. In our experience, irradiation relieved the pain associated with the lesions.

ACKNOWLEDGMENTS: We appreciate the help and co-operation received from many of the members of the surgical and pathological services. We are especially indebted to George S. Baker, M.D., for his permission to include the neurosurgical cases, some of which he has reported orally. We understand that Dr. Baker plans to report the neurosurgical aspects with a follow-up over a longer period of time.

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Congenital Atresia of the Esophagus and Tracheo-Esophageal Fistula[1]

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THE RELATIVELY meager roentgenologic literature on the subject of congenital esophageal atresia has dealt almost exclusively with isolated case reports. The apparent reason why more comprehensive analyses of the subject have not appeared is that, until very recently, this interesting anomaly has been universally fatal and generally regarded as a distinct medical oddity. The condition is relatively uncommon, but through various improvements in surgical technic and postoperative care it has been brought into the realm of surgically correctable abnormalities, and greater interest is being taken in the establishment of its diagnosis. Many of the diagnostic and therapeutic problems which have arisen confront the roentgenologist directly, because it is largely by his methods that the diagnosis of esophageal atresia, the recognition of its complications, and the results of surgical management are graphically recorded. It may be stated justifiably that roentgen examination is essential in the proper management of the condition, especially during the postoperative period.

The purpose of this report is to review the previously described roentgenologic findings in esophageal atresia and tracheo-esophageal fistula, and to present some additional observations made in the group of 46 patients with various combinations of these anomalies seen at the University Hospital since July 1935.

LITERATURE

For excellent embryologic descriptions of the anomalies under discussion, the reader is referred to the articles of Singleton and Knight (1) and of Chont and Starry (2). The anatomic relationships of the usual type of combined esophageal atresia and tracheo-esophageal fistula are shown particularly well in postmortem roentgenograms which illustrate a case reported by Sussman (3). Brennemann's description (4) of the clinical findings in these patients is classical. Comprehensive summaries of the cases reported in the medical literature have been contributed by Plass (5), Rosenthal (6), Strong and Cummins (7), and Ashley (8). Methods of surgical management are contained in the communications of Leven (9, 10), Lanman (11), Ladd (12), Haight and Towsley (13), and others (14–20).

CLASSIFICATION OF LESIONS

Vogt's widely quoted classification of esophageal anomalies (21) has withstood the test of time because it is simple and usable. He lists the following types:

Type I. Complete absence of the esophagus

Type II. Atresia of the esophagus with an upper and lower esophageal segment, each ending in a blind pouch.

Type III. Atresia of the esophagus with tracheo-esophageal fistula.

a. With fistula between upper segment and trachea.

b. With fistula between lower segment and trachea.

c. With fistula between both segments and the trachea.

To this group might be added that form of single tracheo-esophageal fistula which exists without esophageal atresia. This type is unusual and presents particular diagnostic difficulties.

Type III *b* is the most common combina-

[1] From the Departments of Roentgenology and Surgery, University of Michigan, Ann Arbor, Mich. Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

tion of anomalies encountered in the esophagus and trachea. Rosenthal (6) reported the presence of this particular abnormality in 215 of 255 collected cases, an incidence of 84 per cent. In the present series of 46 patients, 42 (91.3 per cent) were in this category. Two patients were found to have agenesis of the lower esophageal segment, one had a single fistula between the esophagus and trachea without esophageal atresia, and in one instance the exact type of anomaly was never accurately determined.[2] Because of the overwhelming predominance of Type III *b*, most of the following remarks will be referable to that type of the anomaly.

CLINICAL FINDINGS

The signs and symptoms of esophageal atresia are quite uniform and fairly characteristic. Inability to swallow fluids, attacks of choking, dyspnea and cyanosis especially during attempted feeding, and intermittent accumulation of mucus in the pharynx with resultant respiratory obstruction constitute a clinical picture that should not go unrecognized. Inability of the examiner to pass a catheter into the infant's stomach will permit a presumptive diagnosis of at least partial esophageal obstruction, but roentgenologic examination is necessary for a positive diagnosis of complete esophageal atresia.

ROENTGENOLOGIC CONSIDERATIONS

Roentgen examination should begin with careful fluoroscopy of the chest in both the anteroposterior and lateral projections without the use of any contrast medium. Following fluoroscopy, roentgenographic exposures are made. These procedures enable the observer to evaluate the status of the lungs more accurately than is possible if opaque material is present in the esophagus or has inadvertently flowed into the tracheobronchial tree. The importance of a careful analysis of the pulmonary status preoperatively lies in the fact that some degree of pneumonia frequently occurs as a result of aspiration of attempted feedings or of secretion within the pharynx or upper esophagus. Because of the blind proximal esophageal pouch, these fluids collect in the upper esophagus and tend to overflow into the lungs through the larynx, producing atelectasis or pneumonic consolidation. These complications are the most important immediate causes of death in patients with esophageal anomalies.

Pulmonary atelectasis may be either of the fetal type, due to incomplete expansion of a portion of lung following birth, or of the acquired type, incident to the aspiration of pharyngeal secretions and feedings into the bronchial tree. Fetal atelectasis occurs most often in the right upper lobe. In this location, indirect signs denoting loss of pulmonary volume usually are not seen on the roentgenogram, although abnormal mediastinal shift on respiration may be demonstrable fluoroscopically. Obstructive atelectasis likewise is more apt to involve the upper portions of the lungs, particularly on the right side. When atelectasis is present, postural treatment may be followed by spectacular roentgenographic changes within a matter of minutes (Fig. 1).

Frequently it is not possible to distinguish atelectasis from pneumonia in these infants, and one has to be content merely to designate that abnormal increase in density is present in one or more lobes. In this series of 46 patients, 45 had anteroposterior roentgenograms of the chest on admission. Abnormal increase in density was observed in the lungs of 27 of the group. The right upper lobe was involved most often, pneumonia, atelectasis, or both, occurring in this region in 22 patients.

Preliminary roentgenologic survey of the chest may reveal occasional associated developmental defects, such as congenital cardiac anomalies. In this group, three such lesions were recognized by x-ray examination (Fig. 2).

In general, the incidence of various extra-esophageal congential defects was

[2] In this indeterminate case, roentgenograms showed definite atresia of the proximal esophagus. Absence of air shadows in the gastro-intestinal tract suggested that no tracheo-esophageal fistula was present, but this was not confirmed, since operation was not undertaken and autopsy was not obtained.

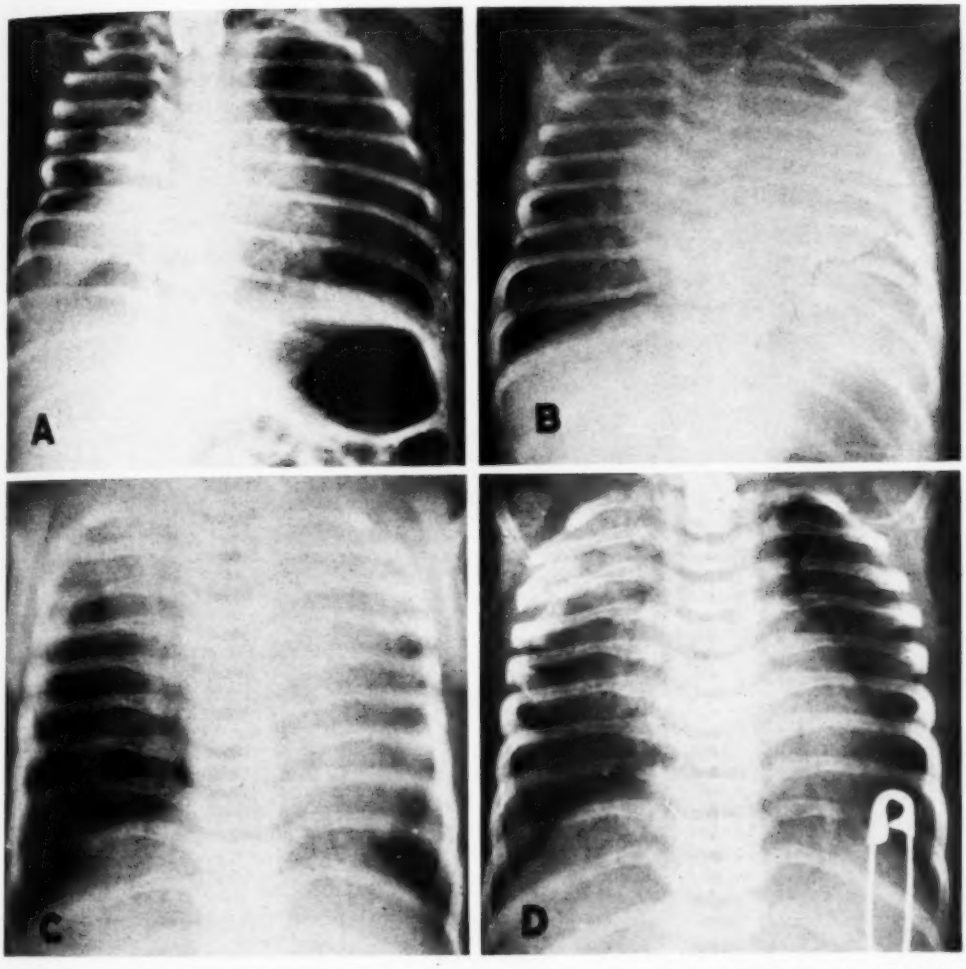

Fig. 1. Preoperative bedside films showing rapid effect of postural change on atelectasis. A. (Case No. 520879). Abnormal density (presumably atelectasis), right lower lobe. Note iodized oil in blind upper esophageal segment. B. Same patient twenty-four hours later. The right lower lobe has cleared but the right upper lobe and entire left lung are now involved. C. (Case No. 522664). Atelectasis of both upper lobes. D. Same patient only three hours later, with complete clearing of left lung. Oil in upper esophagus. (C and D reproduced by permission of *Annals of Surgery*, from Haight, 18.)

relatively low in this series of cases; it did not approach the high rate of occurrence (63 per cent in 149 patients) reported by Plass (5) in his exhaustive review of the literature up to 1919. All but one[3] of the anomalies discovered in our patients, including those found at autopsy, were of a type entirely compatible with life. Ladd (12), on the other hand, encountered a large number of serious malformations in other portions of the body occurring in conjunction with esophageal anomalies.

Diagnosis of Esophageal Atresia Without Use of Contrast Media: Various methods have been described by which a diagnosis of atresia of the esophagus and tracheoesophageal fistula can be made from films alone, without the help of contrast media. Solis-Cohen and Levine (22) state that a lateral projection of the chest may show a

[3] This patient had congenital heart disease with pronounced cyanosis. Operation was not undertaken.

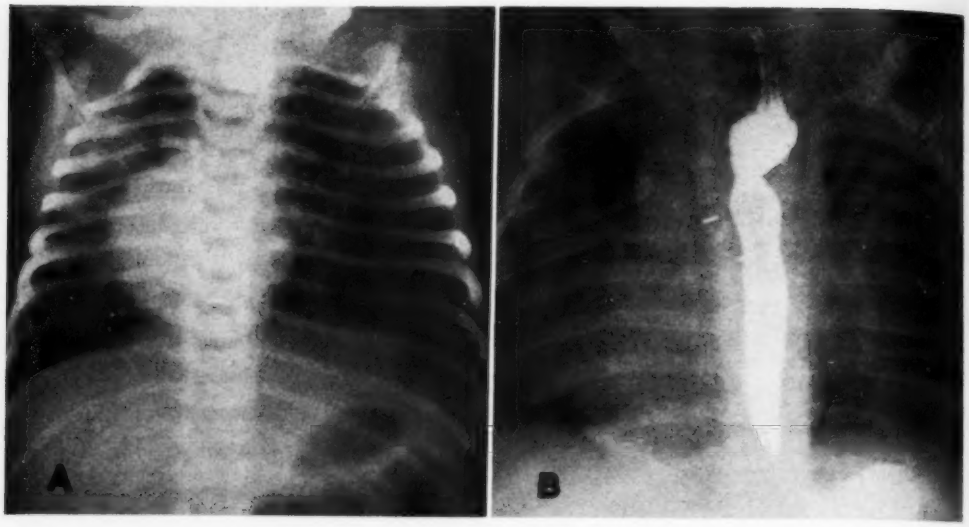

Fig. 2. (Case No. 528008). Congenital esophageal atresia with associated dextrocardia. A. Preoperative film at one week. B. Postoperative film showing reconstructed esophagus six months later. Note shape and position of heart and aorta. (From Haight, 18. Reproduced by permission of *Annals of Surgery*.)

"pencil-like" airway leading from the bifurcation of the trachea to the stomach. This, they maintain, represents the lower esophageal segment filled with air. In addition, they feel that the absence of air in the proximal portion of the esophagus indicates retention of secretions in a blind pouch and therefore is of diagnostic significance.

Fuhrman *et al.* (23) contend that these diagnostic criteria are unreliable, pointing out that normal bronchovascular markings may simulate the "pencil-like" airway; that the lower esophagus may be clearly delineated in an infant without a tracheoesophageal fistula as the result of regurgitation of gas from the stomach; and that the presence of air in the proximal esophagus frequently cannot be seen in the normal infant. In a later article, however, these same authors (24) reported a case of their own in which they observed this controversial airway connecting the trachea and stomach.

Selander (25) reports another sign which may be helpful in the diagnosis of esophageal atresia. He believes that the proximal blind esophageal segment, which is almost always dilated and hypertrophied, will produce a characteristic anterior displacement and narrowing of the trachea demonstrable in the lateral projection.

Of the signs just mentioned, anterior displacement of the trachea with some degree of compression of its posterior margin was the only one found with any degree of regularity in our group of patients. It was seen in 24 (60 per cent) of the 40 patients for whom lateral roentgenograms were made (Fig. 3). The occurrence of air in the proximal esophagus is largely fortuitous, and no great significance should be attached either to its presence or absence unless a dilated, blind upper esophageal segment is completely outlined by swallowed or injected air (Fig. 4). Under such circumstances, it is conceivable that a fluid level might be demonstrated at the base of the pouch if a lateral film were made with the patient upright. We have attempted to show such a fluid level in the last two patients examined, but we have not succeeded. No instance of a lower esophageal airway was recorded and none could be found in a careful retrospective review of roentgenograms.

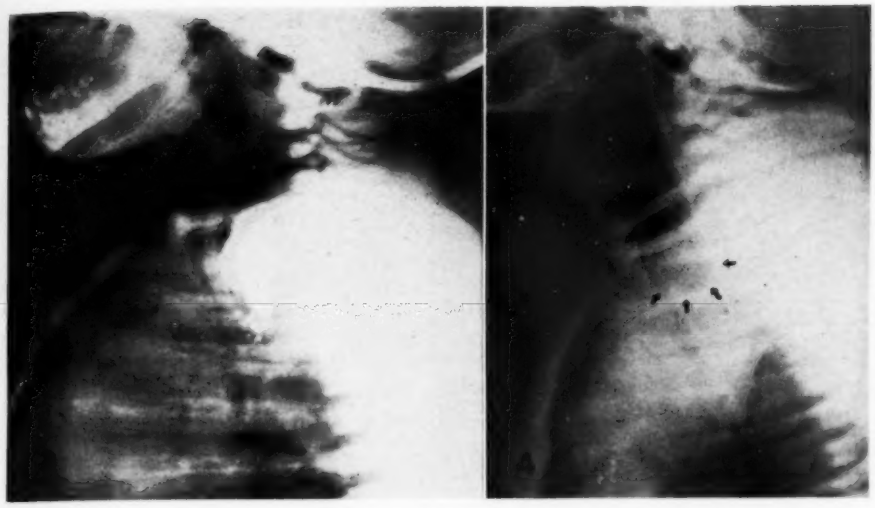

Fig. 3. (Case No. 571090). Anterior displacement and compression of trachea adjacent to dilated, hypertrophied upper esophageal segment, which contains iodized oil and air.
Fig. 4. (Case No. 557442). Dilated proximal esophageal segment completely outlined by swallowed air. Arrows indicate lower margin of blind pouch.

As previously stated, insertion of a small soft rubber catheter (No. 10-12F.) into the esophagus is of value in establishing the presence of obstruction. If the catheter reaches the stomach, as indicated by aspiration of gastric contents, this procedure will quickly rule out the presence of esophageal atresia. If gastric contents cannot be aspirated after the catheter has been introduced sufficiently far to reach the stomach, fluoroscopy with the catheter in place is essential to determine if obstruction has been met in the upper esophagus. The catheter may loop back upon itself (Fig. 5) and, without roentgenologic confirmation in such instances, an erroneous diagnosis of esophageal patency may be made.

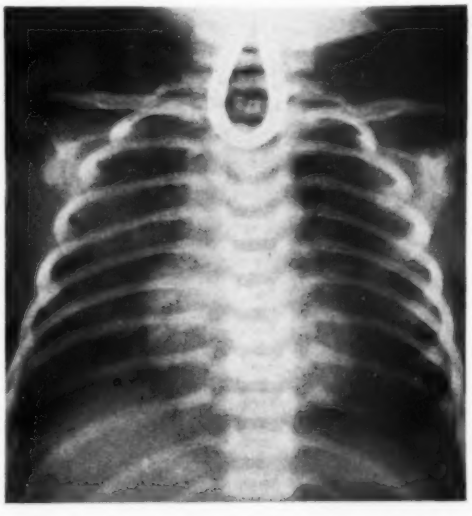

Fig. 5. (Case No. 512466). Characteristic looping of soft rubber catheter in upper esophagus, denoting site of atresia as well as dilatation of upper esophageal segment.

Even under fluoroscopic control, the use of a catheter alone has serious shortcomings, the main one being that it will disclose neither the presence of partial esophageal obstruction nor fistula formation between the proximal esophageal segment and the trachea. Failure to recognize the latter anomaly preoperatively might prove unfortunate, particularly if it occurred in association with an identified fistula between the trachea and the distal esophageal segment. Surgical correction of the distal fistula would not cure the patient because of the persistent proximal tracheo-esophageal communication.

Tucker and Pendergrass (27) have re-

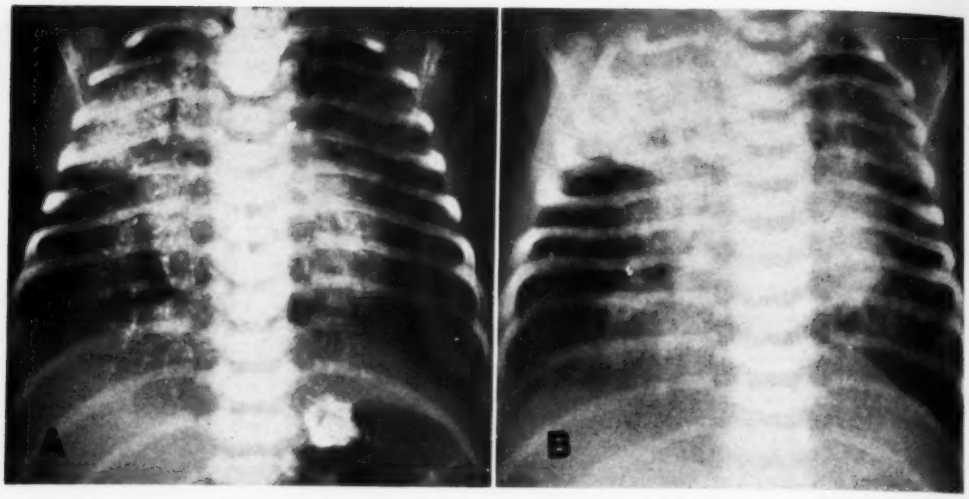

Fig. 6. (Case No. 502704). A. Extensive overflow of iodized oil from upper esophagus into trachea, with resultant aspiration. The opaque medium has entered the lower esophageal segment and stomach *via* the tracheo-esophageal fistula. B. A roentgenogram forty-eight hours later strongly suggests lipid pneumonia.

ported a case of type III *b* anomaly, in which an elaborate and highly accurate modification of the catheter technic was employed for diagnosis. Atresia of the upper esophageal segment was viewed directly through a 3.5-mm. esophagoscope and then confirmed by feeding the infant a thin bismuth mixture and obtaining appropriate roentgenograms. Following withdrawal of the bismuth with a catheter, a 3.5-mm. bronchoscope was passed into the trachea and the tracheo-esophageal fistula was seen. Finally, a small opaque catheter was passed through the bronchoscope into the fistula. Under fluoroscopic control, the catheter was seen to pass into the lower segment of the esophagus and on into the stomach.

Contrast Media: The use of barium sulfate in any form to demonstrate esophageal atresia is unanimously condemned because of the unquestioned irritating effects of this non-absorbable substance should it gain entrance into the lungs.

Fuhrman *et al.* (23, 24) have advocated the use of air as a contrast medium and report a case in which it was employed to good advantage. Under fluoroscopic guidance, a soft rubber catheter was inserted into the esophagus; after the point of atresia was encountered, a few cubic centimeters of air were injected into the proximal esophageal pouch by means of a small bulb syringe attached to the catheter. The dilated, blind cul-de-sac was then observed on the fluoroscopic screen and on subsequent roentgenograms.

The judicious use of bland iodized oil under careful roentgenoscopic control is the most satisfactory method of producing graphic roentgenologic proof of the anomaly. It should be emphasized, however, that the use of oil is not without danger, especially if it is given in an unduly large amount, because of the likelihood of its aspiration into the lungs. Clinically, iodized oil is non-irritating in normal lungs, but Weinberg (26) has convincingly demonstrated histopathologic changes attendant upon its use, particularly in abnormal lungs.

It has been found that the minimal amount of 1.0 c.c. of oil is sufficient for diagnostic purposes, and this small quantity is not likely to overflow into the trachea. Several of the patients in this series were given objectionably large amounts of iodized oil and, in at least one case (Fig. 6), it may have contributed to a lipid pneumonia which proved fatal.

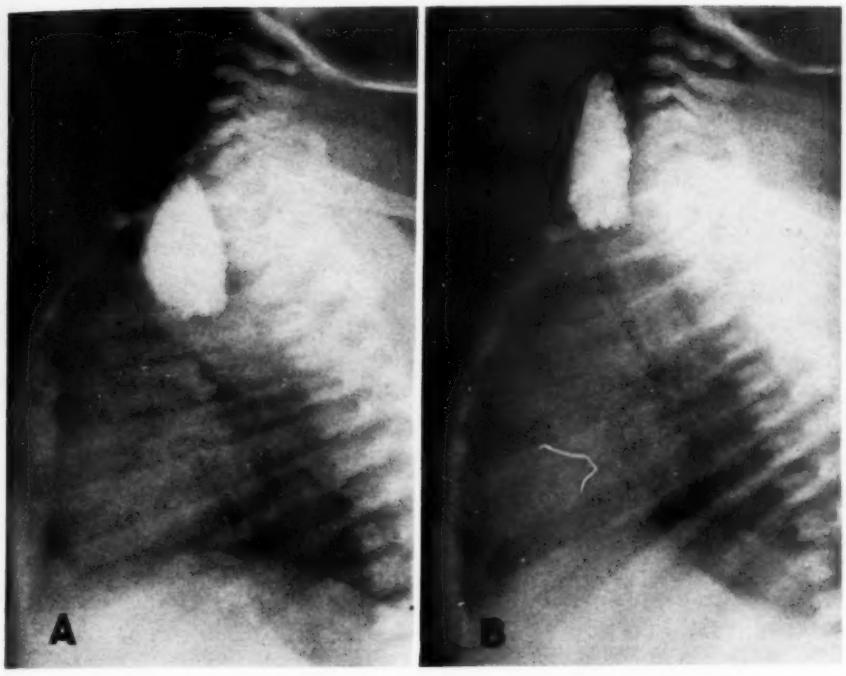

Fig. 7. (Case No. 498016). Effect of respiratory phase on position of atretic upper esophagus. A. Lateral film showing low position of oil-filled pouch at end of inspiration. B. Pronounced elevation of esophageal pouch near end of expiration.

Following instillation of iodized oil into the blind upper esophagus, the infant should be kept in the prone position as much as possible, as there is less chance of aspiration of the opaque substance than there is if the supine position is employed. When films are exposed, they too should be made with the infant prone.

The iodized oil is removed by suction immediately after the roentgen examination. Inspection of the withdrawn fluid and check-up fluoroscopy are precautions to be taken to assure complete removal of the oil.

Experience has shown that, in addition to the establishment of the presence of esophageal atresia, certain other observations are worthy of note. The position and length of the proximal esophageal pouch are of considerable importance and should therefore be routinely recorded. In this respect, fluoroscopy offers a more accurate means of determining the length of the proximal segment than does roentgenography alone. Thus, if one attempts to determine operability solely from the position of the upper segment on a single film, his interpretation is apt to be fallacious (13). Roentgenograms in one case in this group showed the distal end of the proximal esophageal pouch extending only as low as the first dorsal vertebra. At operation, this segment was found to be actually longer than the average, extending almost to the tracheal bifurcation and overlapping the distal esophageal segment. This paradox is due to the fact that the proximal segment, instead of being a fixed structure, moves freely but variably with respiration, descending on inspiration and ascending on expiration (Fig. 7). The amplitude of this rhythmic excursion is of some prognostic significance in so far as feasibility of surgical anastomosis of the esophageal segments is concerned and, therefore, deserves careful evaluation.

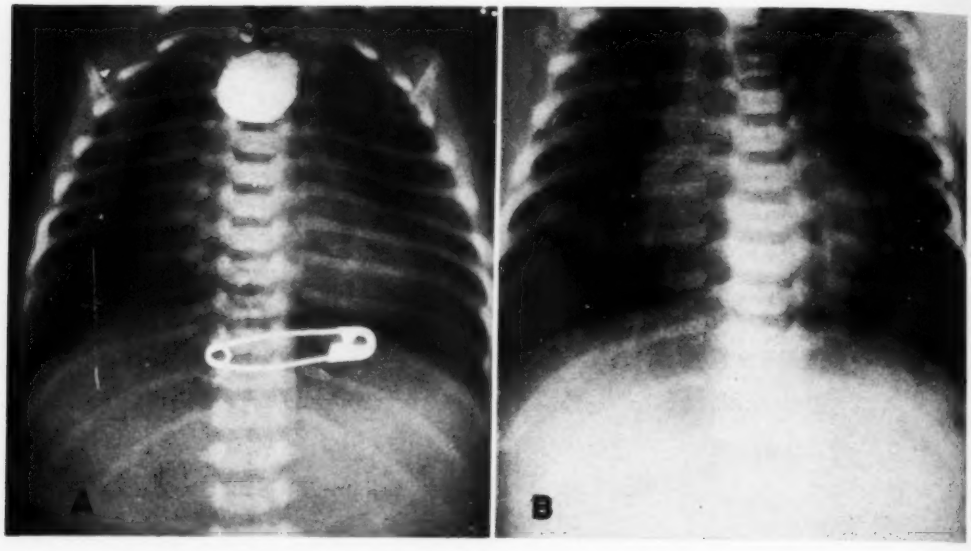

Fig. 8 (Cases No. 487318 and 498016). Congenital esophageal atresia in two infants. Absence of gas in the stomach and small bowel suggested that an associated tracheo-esophageal fistula was not present, but in each instance a small fistula was found at operation.

The movement seldom exceeds the height of two dorsal vertebrae, although in one instance it extended over the vertical height of the first five dorsal vertebral bodies. Unfortunately, no distal esophageal segment was present in this patient and anastomosis was impossible.

Appearance of Stomach and Small Bowel: As mentioned in early case reports, the finding of air in the gastro-intestinal tract of infants with complete congenital occlusion of the esophagus clearly denotes the presence of a fistulous communication between the trachea or bronchus and the lower esophagus. Usually the fistula opens into the mid-line of the trachea posteriorly at a distance of from 0.5 to 1.5 cm. above the carina, although occasionally the esophagus communicates with the carina or a main bronchus.

Failure to visualize air in the stomach or small bowel has been stressed as a sign which indicates absence of a fistula, but this is not invariably true. In 2 of 5 patients who had no roentgenologic evidence of air in the intestinal tract, a narrow fistula was found at operation (Fig. 8).

Unusually pronounced gaseous dilatation of the stomach has been reported as a common clinical and roentgenologic finding in patients with a fistulous communication between the trachea and lower esophagus, but our experience has not proved this to be the rule. Air was present in the stomach and small intestine of 40 of the 45 patients who had preoperative x-ray study, and in only 3 was undue distention of these structures observed. Two of these 3 infants had bilateral pneumonia which may well have been a contributing factor to the distention. Interestingly enough, the patient with the greatest degree of gastric dilatation was the one with a tracheo-esophageal fistula and no esophageal atresia. It should be remembered that the presence of large amounts of air in the gastro-intestinal tracts of newborn infants is entirely physiological.

Hall (28) refers to the possibility of actually observing the stomach distending during inspiration in patients with congenital esophageal atresia and tracheo-esophageal fistula, but states that he could not detect this phenomenon in a case which he reported. We have looked for this sign

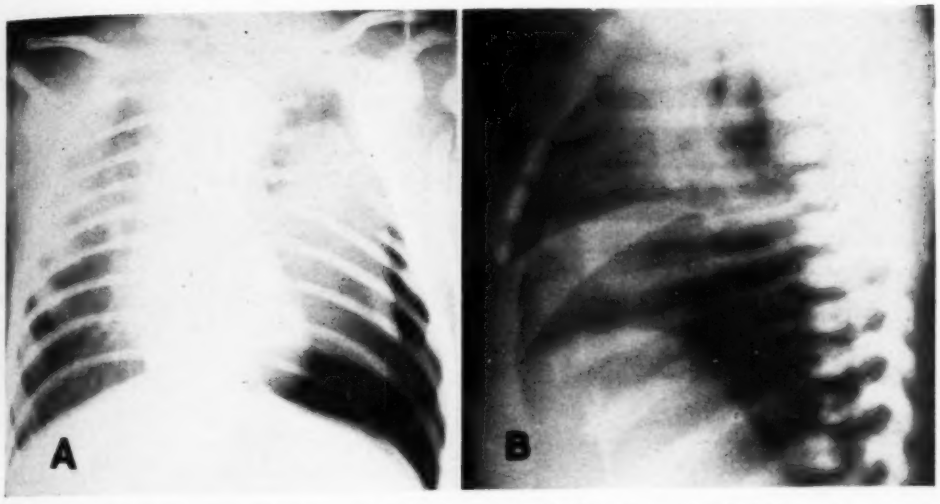

Fig. 9. Clinically unsuspected postoperative pulmonary complications observed on bedside roentgenograms in two different patients. A. (Case No. 519887). Left-sided pneumothorax. B. (Case No. 563843). Atelectasis of right middle lobe. Both abnormalities responded promptly to proper treatment.

only recently but so far have not observed it.

Should iodized oil inadvertently enter the trachea, it may pass through the tracheo-esophageal fistula and lower esophagus and thereby gain entrance into the stomach (Fig. 6, A). If this fact is not kept in mind, the finding of oil in the stomach or small bowel may lead to the wrong assumption that it was swallowed, reaching the gastrointestinal tract through a patent esophagus. Rarely, the lower esophageal segment with its characteristically tapered proximal end will be outlined, but this is undesirable and unnecessary as far as diagnosis is concerned.

Purposeful instillation of opaque medium *via* an intratracheal catheter to outline a fistulous communication between the trachea and esophagus is mentioned only to be condemned. Even with use of the catheter to control the flow of oil, there would seem to be considerable likelihood of the opaque material reaching the alveoli. Furthermore, the procedure is unnecessary for diagnosis.

TYPE OF OPERATION USED

With the exception of the first 3 patients, the type of operation which has been used in most of the cases in this series has consisted of an extrapleural exposure of the anomalous structures, closure of the tracheo-esophageal fistula, and end-to-end anastomosis of the two esophageal segments. This plan has been effected in 26 of 36 patients for whom the operation was undertaken. A roentgenogram of the first case in which the plan was successfully employed is reproduced in Figure 11, A, the operation having been done by one of us (C. H.) on March 15, 1941.

Although the operations in the first patients of this series were done on the left side, a right-sided approach has been used subsequently, because the exposure is thus more easily and safely attained. An extrapleural approach is employed because infants tolerate such exposure much better than surgical procedures which are carried out in the intrapleural space. Temporary leakage at the site of anastomosis may occur postoperatively because of the delicacy of the wall of the lower esophagus and because of unavoidable tension upon the anastomosis. Such leakage is better tolerated if it occurs extrapleurally. With the exception of several of the earlier cases in this series, an endeavor has been made to obtain intrathoracic esophageal continuity in every instance in which it was

at all feasible, even at the expense of temporary leakage of the anastomosis. It is our opinion that better physiologic function can be obtained by this method than by multiple-stage procedures for construction of an extrathoracic esophageal tube.

POSTOPERATIVE OBSERVATIONS

If a pneumothorax has occurred as a result of accidental opening of the pleura at operation, a bedside film should be made at the conclusion of the procedure. Although it is usually possible to inflate the lung completely at the conclusion of the operation, it should be ascertained by roentgen examination that complete expansion has been obtained. This is desirable from the standpoint of improvement of the infant's breathing and the promotion of early adherence of the pleurae at the site of the opening. If residual air is present in the pleural space (Fig. 9, A), it should be removed by aspiration.

Early postoperative pneumonia or atelectasis (Fig. 9, B) may escape clinical recognition, yet be clearly discerned on roentgenograms. In rare instances, a pleural effusion has occurred, and this may be of sufficient magnitude to embarrass respiration. As an effusion is best seen on roentgenograms made in the upright position, all bedside films are customarily made with the infant erect.

Examination of the esophagus with the aid of iodized oil is combined with the bedside examination of the chest on the third or fourth postoperative day. With the infant in the upright position, a small amount of oil (1 or 2 c.c.) is given by mouth from one-half to one minute before the exposure of films. If there is no leakage at the site of the anastomosis and if the oil reaches the stomach satisfactorily, oral administration of fluids in small amounts is begun. Two or three days later the examination is repeated under fluoroscopic control; if the esophagus has remained intact, feedings are rapidly increased in amount.

Distinction should be made between a leak which remains localized to the site of the esophageal anastomosis and one which results in an external esophagocutaneous fistula (Fig. 10). The presence of either does not necessarily condemn the operative correction of the anomaly to failure. An external fistula occurred in 4 of the 9 patients in this series who are living from six months to four and three-quarter years following operation. The fistula closed spontaneously in each instance. Although a stricture developed at the level of the anastomosis in each of these 4 cases, the strictures have responded satisfactorily to dilatation, so that these patients, as well as the other living patients, are receiving all feedings through the reconstructed esophagus.

Persistence of bilateral pneumonitis over a long period of time suggests recurrence of the tracheo-esophageal fistula, or the presence of an additional and unrecognized tracheo-esophageal fistula. Direct evidence of the fistula may be difficult to obtain unless extreme care is exercised in roentgen examination. In this regard, the importance of examining the patient in the prone position following introduction of iodized oil into the esophagus is illustrated by the following case.

A patient in this series developed bilateral pneumonitis postoperatively and it persisted until his death at the age of twenty-five months. Recurrence of the tracheo-esophageal fistula was evident clinically for nine or ten months after esophageal anastomosis, but the fistula appeared to be closing spontaneously. Subsequently, it could not be identified at two fluoroscopic examinations with the patient in the supine position. Failure to visualize the fistula led to the belief that it had completely closed, and the patient was allowed to take all feedings by mouth. The progression of the pneumonitis, however, suggested that the fistula was still patent, and this supposition was finally verified by fluoroscopy. With the patient supine, the fistula could not be seen, but it was immediately evident when an additional swallow of iodized oil was given with the infant lying on his abdomen. Similarly, the one

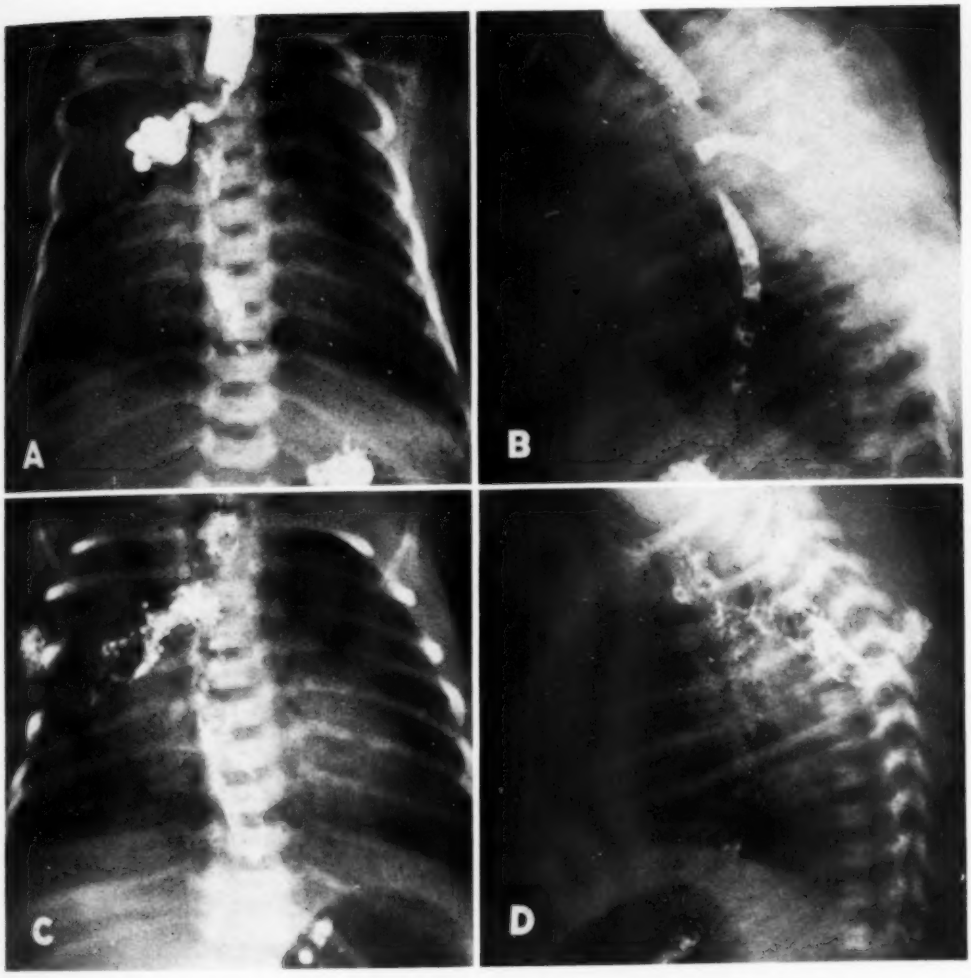

Fig. 10. (Case No. 560928). A and B. Frontal and lateral projections of chest and esophagus three days following repair of esophageal atresia and tracheo-esophageal fistula. Collection of iodized oil at site of anastomosis represents a large local leak. C and D. Re-examination six days later, showing definite signs of external esophageal fistula.

case of tracheo-esophageal fistula without esophageal atresia in this group was not diagnosed by roentgenologic methods because the patient was examined only in the supine position.

When either an esophagocutaneous (external) or a recurrent tracheo-esophageal (internal) fistula develops postoperatively, temporary gastrostomy is indicated. In the event that such a procedure is necessary, the position of the gastrostomy tube is checked fluoroscopically. This is done to avoid the possibility of gastric perforation, which may occur if the tube is inserted too far (3 to 4 cm. is optimum).

Periodic examination of the esophagus is employed for determination of the degree of constriction which may occur at the site of anastomosis. A temporary delay in the passage of iodized oil through the esophagus at the anastomosis has been observed in all instances. The delay is on a mechanical basis, as a result of the narrow lumen in this region. In those infants in whom

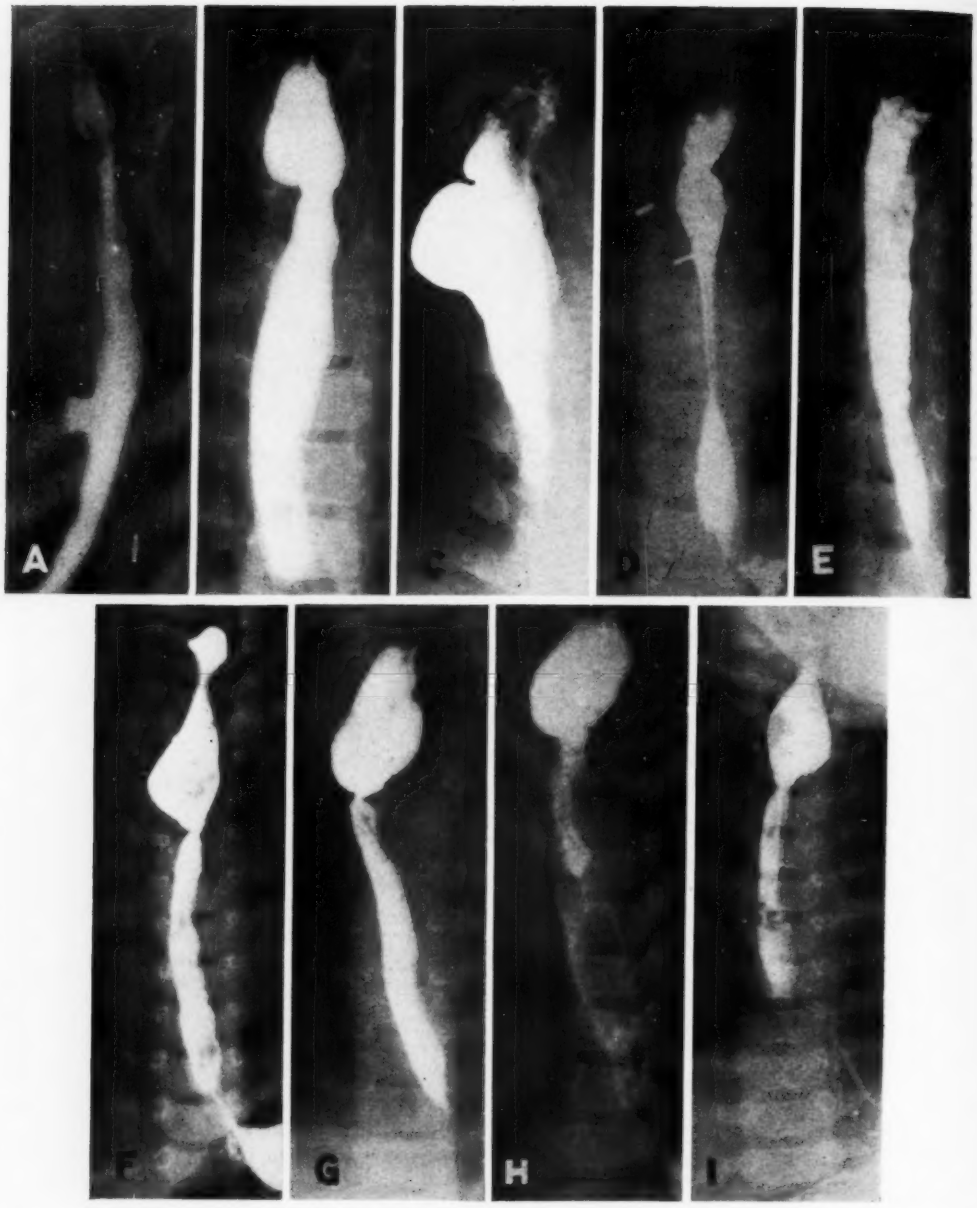

Fig. 11. Roentgenographic appearance of the esophagus in each of 9 patients surviving surgical repair of esophageal atresia and tracheo-esophageal fistula. A. (Case No. 477331). Age of patient 4 3/4 years. Traction diverticulum is due to adjacent calcified tuberculous adenopathy, whch can be faintly seen. B. (Case No. 519-887). Age 34 months. C. (Case No. 522654). Age 32 months. Dilatation of esophagus distal to site of anastomosis presumably due to excessive regurgitation and possible localized weakness in esophageal wall. D. (Case No. 528008). Age 30 months. The visible metallic clips were used for hemostasis at operation. E. (Case No. 533997). Age 26 months. F. (Case No. 555844). Age 14 months. G. (Case No. 563843). Age 10 months. H. (Case No. 564187). Age 10 months. I. (Case No. 571090). Age 6 months.

the anastomosis remained intact following operation, spontaneous enlargement of the lumen occurred as a result of the dilating action of the feedings during swallowing. Actual constriction is particularly apt to occur if there has been an esophageal leak, followed by healing by second intention. Iodized oil has been used for the examination unless it passed through the esophagus too rapidly for accurate evaluation, in which event Rugar provided a more satisfactory means of determining the true width of the esophageal lumen. If dilatation of an esophageal stricture is necessary, roentgen examination again plays an important role in controlling the various dilating procedures and in accurately evaluating the results.

There is considerable variability in the postoperative appearance of the esophagus, not only among different individuals of the group but also in the same patient at different times. Bakwin, Galenson, and LeVine (29) have shown that the normal infant's esophagus is subject to remarkable changes in size and shape, largely due to its inherent distensibility and frequent regurgitation of food from the stomach. When the additional features of congenital malformation and surgical repair are combined with this normal variability, the changes are even more pronounced (Fig. 11). It should be emphasized, however, that in all our patients who have been operated upon for esophageal atresia, the vagus nerve has remained intact. Reestablishment of esophageal continuity has, therefore, been accompanied by relatively normal peristaltic action.

On occasion, the esophagus at the level of the anastomosis may be retracted toward the site of the thoracotomy (Fig. 11). In our experience, this has happened only when there has been leakage at the site of the anastomosis to the exterior with a resultant large extrapleural wound that healed by second intention. In two patients with an external esophageal leak and a small extrapleural wound, there was no retraction of the esophagus.

Although postoperative defects of the ribs are clearly visible roentgenographically, there is little or no over-all deformity of the thoracic cage. The resected ribs regenerate promptly and appear to do so in such a manner that the normal shape of the thoracic wall is maintained. Furthermore, dorsal scoliosis resulting from the operative procedure has not been observed.

SUMMARY

As the anomaly of congenital atresia of the esophagus has now become amenable to surgical correction, the various methods of roentgen examination have assumed added significance in the diagnosis and management of this condition. Experiences derived from a series of 45 consecutive patients with this anomaly, 42 of whom had associated tracheo-esophageal fistula, are discussed. The findings in an additional patient with congenital tracheo-esophageal fistula but without esophageal atresia are mentioned.

Consideration is given to the roentgenologic measures that are valuable for the establishment of the diagnosis of the anomalies, and for evaluation of any complicating pulmonary lesions which may be present. The importance of roentgen examination and the methods of its use in postoperative management are stressed.

Surgical exploration of the anomaly was undertaken in 36 patients of this group, and intrathoracic reconstruction of esophageal continuity was accomplished in 26. The roentgenologic features of 9 living patients who have survived operation for periods of from six months to four and three-quarter years are presented.

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Congenital Partial Atresia of the Esophagus Associated with Congenital Diverticulum of the Esophagus

Report of a Case[1]

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THE PURPOSE OF this communication is to put on record and briefly comment upon, with special reference to diagnosis, a condition which does not seem to have been previously recorded, which, in the absence of precedent, has been termed partial atresia of the esophagus associated with congenital esophageal diverticulum.

CASE REPORT

An illegitimate white male child, 12 hours old, born of a 20-year-old primipara after an uncomplicated labor, was admitted to the pediatric service of the Harris Memorial Methodist Hospital in Fort Worth, Texas, June 25, 1941. He was transferred to the hospital from the foundling home to which he had been brought a few hours after birth at a home for unmarried mothers.

He was extremely cyanotic when first seen and had been in this state, it was learned, from the time of his admission to the foundling home. Physical examination revealed no gross abnormalities, and spinal puncture on the third day of hospitalization showed nothing of significance. Meconium was passed per rectum on the second day.

The child improved transiently after the aspiration of a large amount of mucus from the nose and throat, followed by the administration of oxygen, but attacks of cyanosis continued to recur at irregular intervals, and improvement after the measures mentioned was never more than temporary. No oral feedings were given on the first day of hospitalization. On the second day the oral intake amounted to 30 c.c., and on the third day 43 c.c. The nurse reported that the child choked whenever he was fed and that on the fourth day, although he ate hungrily, he promptly vomited all the milk ingested. The rectal temperature during this period ranged from normal to 103° F.

An attempt at gavage on the fifth day was unsuccessful, the tube being stopped by an obstruction after it had been inserted for a distance of 8 cm. Roentgenologic examination (Fig. 1) immediately following this attempt showed the lungs to be clear and the heart shadow normal in size and position. Air was present in the stomach and small intestine, in about the amount usually present in the alimentary canal in newborn children, and this finding was interpreted as indicating communication between the respiratory and gastro-intestinal tracts. A catheter which had been passed into the esophagus had encountered an obstruction at the level of the third dorsal segment, where the tip turned upward. A second examination (Fig. 2), after the injection of a small amount of opaque fluid through the catheter, showed that the esophagus apparently terminated at this level in a smooth, rounded, blind end. On the basis of these various observations, a diagnosis was made of complete atresia of the esophagus, and it was assumed that a fistulous communication between the respiratory tract and the lower segment of the esophagus existed below the level of the atresia.

Gastrostomy was immediately performed under ether (open-drop) anesthesia. The esophagus was closed with a single silk ligature, and the anterior wall of the stomach was sutured to the peritoneum at the edge of the wound. Postoperative measures included parenteral fluids, oxygen inhalations, and aspiration of mucus which continued to appear in the nose and throat. Attacks of cyanosis continued to be frequent. On the third postoperative day the nurse reported that soon after the child had been fed by way of the gastrostomy opening a small amount of the formula could be identified in the mucus aspirated from the throat. Similar observations were made on the fifth and sixteenth days. On two occasions a bariumized mixture was introduced through the gastrostomy tube but roentgen examination failed to reveal any of the opaque medium in the respiratory tract or in the lower portion of the esophagus. On one of these occasions the nurse reported that some of the mixture was later present in the mucus aspirated from the throat.

The child's condition became progressively worse after operation, and death occurred on the twenty-first postoperative day, the twenty-sixth day of life. A purulent discharge from the abdominal wound occurred for five days antemortem. The rectal temperature, which had frequently been 105° F., was normal for four days before death. Abdominal distention was never marked.

The significant findings at necropsy were reported as follows by Dr. John J. Andujar:

Necropsy: The child was emaciated, the chest wall being so thin that the individual ribs were

[1] From the Harris Clinic and Harris Memorial Methodist Hospital, Fort Worth, Texas. Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

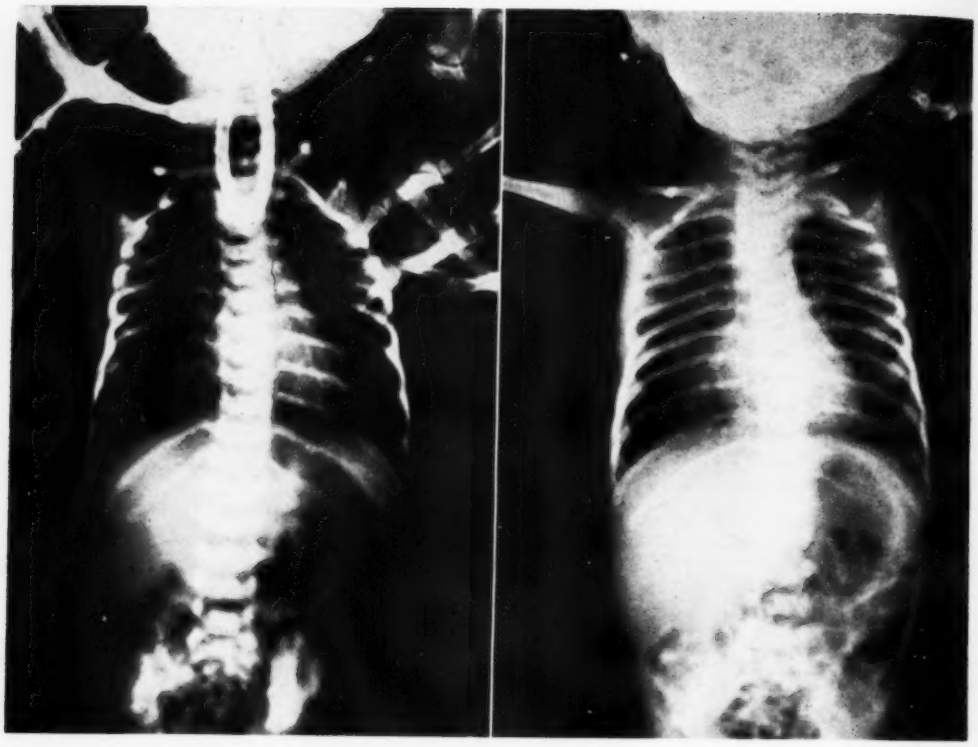

Fig. 1. Film showing catheter introduced into upper segment of atretic esophagus, with its tip turned back at the point of obstruction, demonstrated at necropsy to be the inferior aspect of the diverticulum. Note the air in the stomach and small intestine.

Fig. 2. Film showing upper segment of atretic esophagus filled with barium and apparently terminating in a blind pouch, demonstrated at necropsy to be a diverticulum.

clearly outlined through it. Examination of the cardiovascular system revealed a patent ductus arteriosus. The peritoneal cavity was riddled with abscesses, the largest being in the pelvis and in the right and the left subphrenic region.

On careful search, no evidence of a fistulous communication between the esophagus and the respiratory tract could be found. The upper third of the esophagus, from the pharynx to the level of the third dorsal segment, was normal except for a uniform slight dilatation. At the point of juncture of the upper and middle thirds (Fig. 3) the esophagus ended in a blind pouch. The lower third, which was readily identified by retrograde probing from the gastric side, was normal to the level of the sixth dorsal segment. At this point the esophagus assumed a funnel shape and narrowed sharply After considerable difficulty it was eventually possible, by the passage of a very thin probe, to demonstrate that the canal continued to the level of the second dorsal vertebra, 1.5 cm. above the blind pouch (diverticulum) at which the upper third of the esophagus terminated. At this point the filiform tract communicated with the upper third of the canal by a slit-like, sharply angulated, oval perforation 0.2 cm. in diameter, in the posterior esophageal wall. On the basis of these findings, an anatomic diagnosis was made of congenital partial atresia of the esophagus, associated with congenital esophageal diverticulum.

Section through the esophagus at the level of the diverticulum showed a somewhat thinned-out collagenous stroma, with some round-cell infiltration. The lining of the diverticulum was histologically the same as the lining of the stoma of the esophagus, which was almost completely atretic at this level.

Before the esophagus was sectioned, a demonstration was conducted, which readily explained the nurse's repeated reports of the presence in the aspirated mucus of food and barium introduced into the stomach by way of the gastrostomy tube; no plausible explanation for this observation had previously been advanced. The esophagus was filled with water, a portion of which passed into the diverticulum. It was then observed that the weight of the filled diverticulum completely closed the slit-like communication between the upper and lower segments of the esophagus, but that it immediately

re-opened when the esophageal canal was again empty. These postmortem experiments explained the observations made during life:

(1) No food could pass into the stomach, and none of the injected barium was observed in the stomach, on roentgenologic examination, because the weight of the diverticulum promptly closed the communication between the upper and lower portions of the esophagus as soon as the sac had become weighted down with ingested or injected material.

(2) Gastric contents introduced through the gastrostomy opening could make their way in small amounts through the atretic esophagus and appear in the mucus aspirated from the throat because, when the esophagus and diverticulum were empty, the slit-like communication between the upper and lower portions of the esophagus gaped open. Had the significance of the nurse's observations been realized during life, it should have been possible to reason out the conditions present.

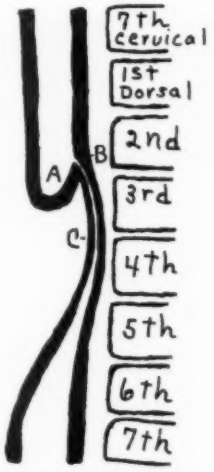

Fig. 3. Diagrammatic lateral presentation of congenital partial atresia of the esophagus with esophageal diverticulum. A. Diverticulum. B. Slit-like communication between diverticulum and esophagus. C. Area of partial atresia.

COMMENT

Credit for the first description of congenital atresia of the esophagus has been variously assigned. According to Singleton and Knight (13), who attribute their data to Mackenzie in 1880, the anomaly was first observed by Gibson in 1696 and was reported by him in a textbook of anatomy published in 1703. According to Ladd (9), who attributes his data to a publication by Mackenzie in 1884, the earliest observation was made by Durston in 1670 and the first case report was published by Martin in 1821. The confusion is typical of the ascription of credit in many other conditions, and the present writer, since he does not have access to the original literature, merely cites the citations.

Congenital atresia of the esophagus is not a common developmental anomaly. According to Mackenzie (9) 42 cases had been reported by 1880. In 1931 Rosenthal (11) collected 255 cases and added 8 of his own. In 1940 Ashley (1) collected 314 examples to which Ladd in 1944 added 72 cases observed at the Children's Hospital in Boston and made the statement that the number of recorded cases must be approximately 400. Although no attempt has been made by the present writer to collect the recently reported cases, a casual review of titles suggests that the number now on record considerably exceeds Ladd's estimate.

The incidence of congenital atresia of the esophagus varies widely. It has been estimated at 1:50,000 cases but is naturally very much higher in children's hospitals, where the material tends to be highly selective. On the other hand, Fuhrman and his associates (4) did not see a single instance in 12,285 deliveries on the maternity service of the Metropolitan Hospital in New York, where the proportion of autopsies on newborn infants is so high that it was considered unlikely that any cases had been overlooked. The present writer has observed 4 cases, including the one reported in this communication, over a period of twenty-three years. It seems scarcely necessary to emphasize that the relatively large series of cases recorded recently, as compared with the individual cases or small groups of cases formerly reported, merely indicate an increasing awareness of the condition and not a true increase in incidence.

Congenital narrowing of the esophagus, as distinguished from complete esophageal atresia, is apparently extremely rare. Beatty (2), after a systematic search of the literature, could find only 57 cases, includ-

ing 2 personally observed examples, reported up to 1928. In his communication he noted that only 2 instances were observed at the London Hospital in 13,201 necropsies performed between 1907 and 1921. He also noted that Hirschsprung, who selected congenital narrowing of the esophagus for the subject of his thesis for his medical doctorate in 1861, in spite of his interest in the subject did not have a single case under his care until thirty-four years later. Whether all of the cases collected by Beatty were instances of congenital narrowing of the esophagus is perhaps open to doubt, since his series included not only infants but also children and adults, one of whom was eighty-four years of age.

To the very unusual instance of congenital partial atresia of the esophagus reported in this communication must be added the even more unusual presence, in association, of a congenital esophageal diverticulum. So far as can be determined by a search of the titles in the recent literature, as well as by the investigation of numerous individual articles, this is only the second instance of the latter congenital anomaly to be reported. It occurred, furthermore, in a newborn child, whereas the only other instance on record, reported by Jackson and Shallow (8) in 1926, occurred in an eight-year-old child, though there seems to be no doubt that it also was congenital. The case of esophageal "diverticulum" reported by Holderman (6) in 1927, in association with congenital atresia of the esophagus and tracheo-esophageal fistula, seems from the description and illustrations to be an instance of faulty nomenclature, the so-called diverticulum apparently being merely the blind upper end of the atretic esophagus.

The multiplicity of abnormalities represented in the reported case, namely, partial atresia of the esophagus, diverticulum of the esophagus, and patent ductus arteriosus, is not at all unusual. In Holderman's (6) case, for instance, the child, in addition to the esophageal anomalies, had 13 ribs on each side and a double uterus. Poth (10) reported a case of patent ductus arteriosus associated with congenital atresia of the esophagus. In 49 of Ladd's (9) 72 cases the esophageal anomalies were associated with one or more other abnormalities, which involved the heart and aorta in 10 cases and which in many instances were incompatible with life. In Humphreys' (7) series of 27 cases only 10 associated anomalies were present, and in only one case were they of sufficient severity to influence the outcome, but this is not the usual experience.

In this connection certain privately published data collected by D. P. Murphy (12) are of interest. His study of 890 congenital malformations led him to the following conclusions: Malformation of some sort occurs in 1 of every 213 individuals born alive. The incidence is twice as high in white as in Negro children. Almost a quarter of malformed children present more than one anomaly. The frequency of birth of a subsequent malformed child is 25 per cent greater in families already possessing a malformed child. The older the mother, the greater is the possibility of a malformed offspring. Approximately 25 per cent of all malformed children are stillborn, and about 90 per cent, including those born dead, do not live beyond the first year. Ignorance of the family history in the case reported herewith prevents comment upon these conclusions in relation to it.

Of the several classifications of congenital anomalies of the esophagus, Vogt's (15) is the simplest and most useful. It can be summarized as follows:

1. The esophagus is completely absent.
2. The upper portion of the esophagus ends in a blind pouch in the region of the first or second dorsal vertebra. The lower segment originates in a blind pouch at the level of the fourth or fifth dorsal vertebra.
3. The esophagus is atretic, as in type 2, and communicates with the trachea (A) by way of the upper segment, or (B) by way of the lower segment, or (C) by way of both segments.

Complete absence of the esophagus

(agenesis) is extremely rare, and type 3B or 3c occurs in probably 80 per cent of all cases. It will be noted that the case reported in this communication does not fall into any of these classifications.

Beatty (2) classified congenital partial atresia of the esophagus into two groups. In the first, a thin diaphragm of mucous membrane stretches across the interior of the tube and is perforated by an opening varying in size and usually situated eccentrically. In the second type, as in the case reported in this communication (without regard to the presence of the diverticulum), the esophagus is narrowed longitudinally for a variable distance and to a variable degree. All the coats of the esophagus, according to Beatty, are normal in structure, thickness, and histologic aspect, and the anomaly is merely in the size of the canal. In the case reported herewith, the histologic findings varied somewhat from the usual histology of the esophagus.

Until very recently, congenital anomalies of the esophagus were of little more than abstract interest, and Brennemann's (3) opinion, expressed in 1918, was the prevailing one. These children, he wrote, either have bronchopneumonia when they are first seen or it will develop if the anomaly is not corrected. Operation to close the esophagus is not feasible, and in the absence of closure, life, even if it were possible, would be intolerable. The child, for pediatric reasons, could not live even if operation were done, no matter how he were treated. Therefore, after council with the parents, he should be permitted to die as peacefully and as painlessly as possible, and the physician who arrives at that decision has no reason to lose any sleep over it.

The excellent reviews of the literature by Singleton and Knight (13) and by Humphreys (7) indicate that up to the last few years that pessimistic point of view was fully justified. Recent reports of relatively large series of cases (5, 7, 9), however, have completely reversed it. Humphreys' review of 59 operations shows 19 survivals, some for periods of four years, in addition to 5 survivals reported by Leven in an unstated number of operations. Sixteen of the survivals occurred in cases treated by mediastinal ligation, creation of a cervical stoma, and gastrostomy, in which group Leven's 5 survivals are included; 8 occurred in 25 cases treated by direct anastomosis. Haight (5) later reported an additional survival after operation by this technic. Direct anastomosis, when it is feasible, is the more desirable procedure; the other, as Humphreys notes, offering a considerable problem in reconstructive surgery.

These promising results, of course, cannot be achieved, and surgery cannot be undertaken, in these unfortunate children unless the condition is recognized. Moreover, it must be recognized promptly, for respiratory complications, particularly aspiration pneumonia, develop promptly and are enhanced by the aspiration of gastric contents which pass upward through the esophagus into the lung through the fistula into the trachea. The latter difficulty, because of the atresia present, was not a problem in the writer's personal case, in which pulmonary complications were also prevented by the frequent use of suction to remove mucous secretions. The surgical prognosis, generally speaking, depends upon whether or not pneumonia develops before operation is undertaken. Feeding, as Humphreys (7) emphasizes, is no longer of the importance it once was, since a child who is born fairly well nourished can be kept alive for a long period of time by intelligent parenteral alimentation.

The diagnosis of congenital atresia of the esophagus should be suspected on clinical grounds during the first few hours of life if the child suffers recurrent attacks of coughing, choking, or cyanosis, and if quantities of mucus are present in the upper air passages and promptly re-accumulate after aspiration. These attacks are exaggerated when fluids begin to be taken by mouth. Clinical diagnosis must be supplemented by roentgenologic methods, to determine the type of anomaly present.

The upper segment of an atretic esophagus can easily be demonstrated by the passage of a catheter down to the point of the obstruction, followed by the injection into the tube of a few cubic centimeters of air. The lower segment of an atretic esophagus is much less easily demonstrated. In occasional cases it may be outlined by air regurgitated from the stomach in the course of the examination, but the coincidence obviously is purely accidental and cannot be relied upon. Tucker and Pendergrass (14) described a method by which an opaque medium is introduced into a ureteral catheter which has been passed down a bronchoscope through the fistula in the trachea into the lower esophageal segment. Even with this precaution, however, the use of a contrast medium seldom furnishes enough additional information to compensate for the risk its use involves. If it is used, bland iodized oil is preferable to a barium mixture, and whatever material is used should be promptly removed, to prevent its entrance into the lower respiratory tract.

It is generally accepted that the demonstration of a blind upper esophageal pouch by means of air or of an opaque medium is diagnostic of esophageal atresia, with or without communication with the trachea, while the presence of air in the gastro-intestinal tract is diagnostic of a communication between the lower segment of an atretic esophagus and the trachea, or of both esophageal segments and the trachea. The case reported herewith suggests that this conclusion should not be accepted without reservations. The apparent demonstration of a blind termination of the upper esophagus, plus the presence of air in the gastro-intestinal tract, fulfilled the diagnostic criteria for atresia of the esophagus with a tracheo-esophageal fistula, but the conclusion, as necropsy proved, was in error. The nurse's observation, as already pointed out, of gastric contents in the mucus aspirated from the upper air passages was the clue to the diagnosis, and, if properly appreciated, might have led to a theoretic reconstruction of the conditions present. Gastrostomy, which was done as a palliative procedure, did no harm under the circumstances, but a more extensive operation might readily have led to a faulty correction of the anomalies. The child could probably not have lived, regardless of what was done, because of the extent of the atresia, though the correction of the esophageal diverticulum was perfectly feasible.

In retrospect, it seems that esophagoscopic examination might have contributed to the diagnosis in this case, by demonstrating the slit-like opening, which would have suggested the presence of the atretic area. The routine use of this method in all presumptive atresias of the esophagus would do no harm and might be of considerable diagnostic value.

SUMMARY

There is put on record the case of an infant seen twelve hours after birth with a train of symptoms and signs suggestive of congenital atresia of the esophagus with tracheo-esophageal fistula and managed on that assumption. Autopsy revealed the presence of two congenital anomalies of the esophagus which do not seem to have been reported previously in combination and which do not fit into any of the classifications which have been suggested. In the absence of precedent, the condition has been termed congenital partial atresia of the esophagus associated with congenital diverticulum of the esophagus. The literature indicates that partial atresia of the esophagus is very rare, and, so far as can be determined, this is only the second instance of congenital diverticulum of the esophagus to be recorded. No record of a similar case could be found.

Diagnostic considerations are discussed, and their importance is emphasized in view of the great improvement recently achieved in the surgery of congenital esophageal anomalies.

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Roentgen Rays in the Prevention and Treatment of Infections[1]

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IMMEDIATELY after the discovery of x-rays by Roentgen, the study of their effects on various infections was started and this has continued to the present day. At this time, a brief review of the available experimental and clinical data will enable one to appreciate how closely these observations parallel and support one another in their most important aspects. When this is done, a better understanding of the entire problem is certain, and much of the confusion, real or assumed, of the last few years is eliminated.

EXPERIMENTAL STUDIES

As early as 1904, Heineke (1) had shown that many cells react to roentgen rays and that there is an elective action of the rays upon the lymphoid tissues. This was corroborated by Warthin (2) in 1906. Later Desjardins (3) and Pordes (4) also made investigations in this field and expressed the belief that the striking effect of radiation in inflammation is due to the early destruction of the leukocytes, which set free protective ferments, antibodies, and other substances at the site of inflammation more quickly than occurs normally in the natural course of inflammation.

Heidenhain and Fried (5) brought out by serological experiments that these cellular changes are associated with an increase in antibodies in acute infections and proved that the exposure of patients to roentgen rays is followed by a direct increase in the bacteriolytic power of the blood lasting from two to six days. Thus, many years ago, there was experimental evidence that x-rays acted on living cells and caused an increase in antibody formation.

In 1940, Altemeier and Jones (6) reported their observations on the prevention of peritonitis in rabbits by x-rays. This study was undertaken because the authors had observed an immunity against peritonitis in patients who had received irradiation prior to surgery for cancer of the rectosigmoid. They thought this effect of the rays was non-specific, since many organisms were involved, but no infection of any kind occurred. They offered no explanation for the results they obtained. Rigos (7), however, treating experimental peritonitis in guinea-pigs, noted differences in cell changes at various periods after irradiation. Further studies along this line may produce an explanation for the observations of Altemeier and Jones, who had found evidence of immunity some weeks after irradiation.

Bisgard, Hunt *et al.* (8), in 1942, reported work which showed beyond any question that x-rays exerted an antitoxic effect on toxins of bacterial origin; that through this antitoxic effect some degree of immunity could be established for a time; that the antitoxic effect was non-specific in character and that a latent period of a few hours was present before the x-rays were effective.

Thus throughout a period of practically forty years, there has been a worth-while consistency in the findings of many research workers in this field to support the contention of many clinicians that x-rays are of value in the prevention and treatment of infections.

Among the significant facts brought out by these research workers are the following:

(A) After irradiation with x-rays, the lymphocytes and probably other cells give off a protective or antitoxic substance effective against toxins of bacterial origin.

(B) Since the lymphocytes and probably other cells give off this antitoxic substance following irradiation, it is obvious that the presence of living tissue is essential

[1] Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

if any effect is to be produced by the x-ray.

(c) A latent period of several hours is present before the x-rays are effective.

(d) The period of effectiveness of the x-ray is apparently limited, and this period of limitation may depend on factors not yet understood. In the dosage commonly used in infections, it is between the second and the seventh to tenth day.

(e) This antitoxic effect is apparently non-specific in character.

Other experimental data tending to support the work of the foregoing observers, but usually interpreted to the contrary, follow:

Irradiation of Toxins in vitro: The antitoxic effect of the x-ray in patients in the advanced stages of gas infection was so striking that it led us to attempt to neutralize toxins *in vitro*. With no variation in our technical procedures, however, were we able to influence the strength of the toxin *in vitro*. Since it appears that the antitoxic factor is produced by the tissues of the irradiated animal, and as such tissues are absent in this type of experiment, this result was to be expected.

Irradiation of Bacteria in vitro: It was agreed by the early research workers that the pathogenic tendencies of bacteria when irradiated *in vitro* were not affected by radiation in amounts which were much beyond the dose range employed therapeutically for infections. Since no tissues are irradiated in these experiments, no antitoxic factor is produced, and, therefore, no effect of irradiation on bacteria can be expected.

Experiments such as the two discussed above have been interpreted by Weed *et al.* (9) and Erb and Hodes (10) as evidence that x-rays are of no value in treating gas gangrene, whereas actually they add to the already convincing evidence that living tissue must be present if antitoxin is to be liberated. At any rate, it should be obvious that the conditions under which these experiments are carried out are so far removed from those present in the treatment of infected tissues in man that no certain interpretation as to the value of x-rays in that respect seems warranted.

Irradiation of Small Animals Which Live Only a Few Hours after Inoculation: The failures in this type of experiment (Caldwell and Cox, 11; Singer, 12; Kelly *et al.*, 13–15) also support the conclusion that time is a factor in the production of the antitoxic effect. Unless the small animal, which is very susceptible to the toxins, is irradiated some time prior to inoculation, as shown by Bisgard *et al.* (8), it will die in a few hours. Such results lend support to the research work which shows that twenty-four to forty-eight hours must elapse before the antitoxic factor becomes effective.

Irradiation of Larger Animals: Merritt, Den, and Wilcox (16), using sheep at the suggestion of Dr. Sarah Stuart of the National Institute of Health, Washington, D. C., inoculated the animals with a strain of *Cl. welchii*, designated as S.R. 12, the same organism used by Weed (9), and proved everything in these experimental animals that had been claimed for the use of x-rays in treating gas gangrene in man, namely, that they localized the infection, thereby conserved tissue, lessened the toxemia, and lowered the mortality. Although toxins, as well as organisms, were introduced at the time of the inoculation, these larger animals are apparently able to withstand the shock associated with this procedure for a sufficient length of time to permit their cells to respond to the x-rays and produce their own life-saving antitoxin. Such has never been the case with small animals irradiated after inoculation; these die in a few hours, before the x-rays have time to take effect.

From the foregoing experimental data, it is obvious that certain factors must be present in order to secure the beneficial effects of irradiation in the prevention of wound infection or the treatment of acute toxic infections such as gas gangrene: the tissue factor, the dose factor, and the time factor.

(*a*) *The Tissue Factor:* Since the beneficial effect of x-rays is dependent on the liberation of an antitoxic substance formed in the tissues, living cells must be irradi-

ated. Therefore, a fairly large area of tissue should be treated.

Kaplan (17) emphasized the necessity for irradiation of tissue in his recent excellent review by stating: "The associated living tissue activity is essential for the production of the curative effect of irradiation, and for this reason the theories based only on laboratory test-tube investigation are not entirely applicable to human conditions."

(*b*) *The Dose Factor:* Since the beneficial effect of x-rays on the tissues is not apparent until a certain amount of irradiation has been given, and this effect is not increased beyond a certain point, regardless of how great the amount administered, it is evident that a proper dose of x-rays is essential. This dose varies under different circumstances.

(*c*) *The Time Factor:* Since several hours must elapse before the irradiated cells liberate the antitoxic substance, a required period of time must be allowed to elapse before any beneficial effect of the x-rays is to be expected; they are apparently not effective beyond the seventh day.

When any of these essential factors is absent, no beneficial effect of the x-rays appears, as shown by the experiments just discussed, demonstrating the failure to neutralize toxins *in vitro*, the failure to influence the pathogenic effect of bacteria *in vitro*, and the failure to cure those research animals which die in a few hours after inoculation or are inoculated or become toxic after the period of effectiveness has passed.

On the other hand, when the three essential factors are present, the following important conclusions are fully supported by the experimental evidence:

(*a*) An antitoxic factor against toxins of bacterial origin is developed by irradiation of living tissue.

(*b*) This antitoxic factor is non-specific in character and, therefore, is of value in prophylaxis and treatment of many infections during the period of its effectiveness, which is from the second to about the seventh day.

CLINICAL STUDIES

In any clinical application of x-rays for the prevention or treatment of acute infections, it is obvious that two of the essential factors (living tissues and x-rays) are always present, at least in some degree, while the third, the time factor, may or may not be present, since the patient may die shortly after the x-ray treatments are started.

(*a*) *The Tissue Factor:* Whether or not some of the failures in the clinical application of the rays may be attributed to an error in the amount of tissue irradiated is not easily determined, but it has been the observation of many radiologists that when a fairly large area, including some normal tissue about the region infected, was irradiated, the best result was secured.

That the tissues of man produce an antitoxic substance similar to that produced in Bisgard's experiments on rabbits is evident clinically and statistically from the observations made on the treatment of gas gangrene. This disease is selected for comparison because it belongs in that group of toxic infections for which claims have been made for the value of x-rays in prevention and treatment and because more complete data are available in the literature on this than on any other infection.

Clinically, the antitoxic effect (15, 18, 19, 20) of the x-rays in a well established gas infection is so impressive that it cannot be missed by anyone. Statistically, there is a consistently lowered mortality rate in the various clinical types of gas infections which received no commercial antitoxin as compared with the cases treated with the addition of commercial serum. The very lowest mortality recorded, 4.34 per cent, was in a group of 46 cases receiving three or more x-ray treatments and no commercial serum (15). Thus, it is evident clinically and statistically that, whether or not an antitoxic substance is produced in human tissues as a result of x-rays, the effect with x-rays is essentially the same or better, which is the important fact for any clinician. As a rule, no commercial serum is necessary

if x-rays are used. In fact, if x-rays are used in the suspected or early stages of the disease, there is an advantage in omitting commercial serum and depending upon the patient's ability to develop his own antitoxin.

There is, however, an exception to this general rule. We refer to the patient in whom gas infection follows a hypodermic injection (20). In such cases death often ensues so promptly (because toxin is quite likely introduced at the time of injection) that, if commercial serum is immediately available, it should obviously be used in the hope that it may match the invading bacteria and therefore have some effect in the early hours of the disease before the x-rays become effective. We have felt for some time that the multiplicity of organisms involved in so-called gas gangrene is the main difficulty which prevents the preparation of a serum producing consistent results. Serum, if available, might also be used for the patient with advanced disease who has had no x-ray therapy and who looks as though he might die in a few hours, before x-rays have a chance to produce any antitoxic effect in the tissues. Only a moderate dose of commercial serum should be used in any instance.

One would expect an autogenous serum to be free of any toxic reactions such as often follow the use of commercial serum, and this appears to be the case, as no serum sickness was observed in patients who received x-ray treatment alone, while it is a common occurrence in those who are given commercial serum. At any rate, it is universally acknowledged that the ideal means of prevention or treatment of a lethal infection, such as diphtheria or tetanus, is the use of an effective serum; therefore, what could be more desirable than to use x-rays to produce from the patient's tissues a nonspecific antitoxic factor effective against an acute toxic infection, regardless of whether it is called an autogenous serum, an antitoxin, or by any other name? If suspected and early cases received x-ray therapy, the occasion for using any commercial serum would be rare indeed. Further investigation may show that it is never needed under any circumstances, even for those we have suggested as possibilities.

(*b*) *The Dosage Factor:* Experimentally and clinically, it seems that a filtered (filter for safety) dose of x-rays, totalling about 100 r, is adequate, and the number of doses will depend on the clinical course of the case. They are usually given at twelve- to twenty-four-hour intervals through a period of one to five days. Since many variations in the amount of tissue irradiated and in the dosage given are evident in clinical reports on the successful treatment of numerous types of infection, it is obvious that the exact technical requirements to assure the best effect from the use of the first two essential factors are not so sharply defined as in the case with the third, the time factor.

(*c*) *The Time Factor:* The importance of the time factor and its lack of latitude if success is to be obtained is clearly demonstrated in the clinical reports available for analysis in gas gangrene. The technic we recommended called for a treatment every twelve hours. Our statistics (18) show that among those who lived only long enough to receive one treatment (twelve hours) the mortality rate (48.27 per cent) is essentially the same as in the A.E.F., in World War I (48.52 per cent). Those who lived long enough to receive two x-ray treatments (over twenty-four hours) showed a mortality of 28.94 per cent; and among 288 who lived long enough to receive three or more treatments (over thirty-six hours), the mortality dropped to 5.9 per cent.

It is evident, from the foregoing figures, that little or no effect was secured in the early hours after irradiation was begun, but after twenty-four hours the effect was good, while after thirty-six to forty-eight hours it was tremendous. This is what would be expected from the experiments showing that time is a factor in the development of the antitoxic effect. This clinical observation led us to demand early treatment, even before the disease becomes fully established if the best results are to be

secured. In fact, we stated that all contaminated wounds in which a gas infection might be expected to develop should be given a prophylactic treatment each day for three days. We have done this for years and have never had a gas infection develop following this procedure. As a guide to the type of case in which x-ray prophylaxis is indicated, we have stated that any patient thought to need antitoxin to protect against tetanus should also receive x-rays to protect against gas and other rapidly growing organisms.

That it is essential, however, to give antitoxin to protect against tetanus and not to depend on x-rays was determined very early in our study by the occurrence of tetanus in patients recovering from gas gangrene after irradiation. Tetanus may occur in the third and fourth week and apparently is not prevented by the x-ray therapy given for gas infection during the first week. This also supports the observation that the immunity following x-ray therapy does not extend so long (Fig. 1) or is not effective at that time.

Thus, there is clinical as well as experimental evidence that the time factor is essential. The death rate was the same in patients who received only one x-ray treatment as it was in those who received no x-ray therapy, usually because they died before it was time for them to receive their second treatment, or in the first twelve hours, while those who lived into the twenty-hour and thirty-six-hour periods, when the antitoxic effect was present, showed remarkable response to irradiation. The occurrence of tetanus in patients who were treated with x-rays and recovered from gas gangrene also confirms the experimental data which show that the effectiveness of the antitoxic substance formed as a result of x-ray therapy does not extend beyond about the seventh day.

The *non-specific character* of this antitoxic factor, proved experimentally by Bisgard and his colleagues, has also been evident clinically for many years in the treatment of erysipelas, surgical mumps, pneumonia, and other acute toxic infections, as well as in the treatment of gas gangrene and acute spreading peritonitis following appendicitis. Reports on the x-ray treatment of these various diseases extend over too long a period of time and come from too many sources to warrant any legitimate doubt as to their authenticity or their accuracy.

TABLE I: RECENT REPORTS OF POST-TRAUMATIC GAS GANGRENE

Reports	Cases	Deaths
McMILAN, K. D.: Gas Gangrene. West. J. Surg. **51:** 187, May 1943	13	4
BERTOGLIO, J. S., AND RATLIFF, R. K.: Gas Gangrene of the Scrotum. Urol. & Cutan. Rev. **47:** 352, June 1943	1	0
SCOTT, R. K.: X-ray Therapy in Treatment of Gas Gangrene. Royal Melbourne Hosp. Clin. Rep. **13:** 41, December 1942	15	1
TURNER, J.: Gas Gangrene, Royal Melbourne Hosp. Clin. Rep. **13:** 31, December 1942	10	1
WARFIELD, J. O., JR.: Etiology and Treatment of Gas Gangrene. M. Ann. District of Columbia **11:** 175, May 1942	1	0
CALDWELL, G. A., AND COX, F. J.: Roentgen Ray Treatment of Gas Gangrene. Ann. Surg. **114:** 263, August 1941	1	0
HALFORD, F. J.: Gas Gangrene and Tetanus. Hawaii M. J. **1:** 169, January 1942	11	0
DAVIDSON, A. M.: Deep X-ray Treatment of Gas Gangrene: Recovery. M. J. Australia **1:** 557, June 19, 1943	1	0
GOLDMAN, L. B.: Irradiation in Infections. New York State J. Med. **42:** 1341, July 15, 1942	5	1
	58	7

In this recent series of 58 cases with 7 deaths, the mortality rate is 12 per cent, which is less than 1 per cent higher than the mortality of 11.7 per cent for 392 previously collected cases of post-traumatic gas gangrene.

Consistency of Clinical Data on Gas Gangrene: Our report (15) in 1941 showed in Figure 2 and Table III a total of 392 cases of post-traumatic gas gangrene from various sources, with 46 deaths, or a mortality of 11.7 per cent. A recent hurried review of papers published in English and listed in the *Quarterly Cumulative Index Medicus* and available to the writer (see Table I) brought out 9 more reports (from entirely new sources) totalling 58 cases, with 7 deaths or a mortality of 12 per cent, less than 1 per cent difference from the former mortality rate.

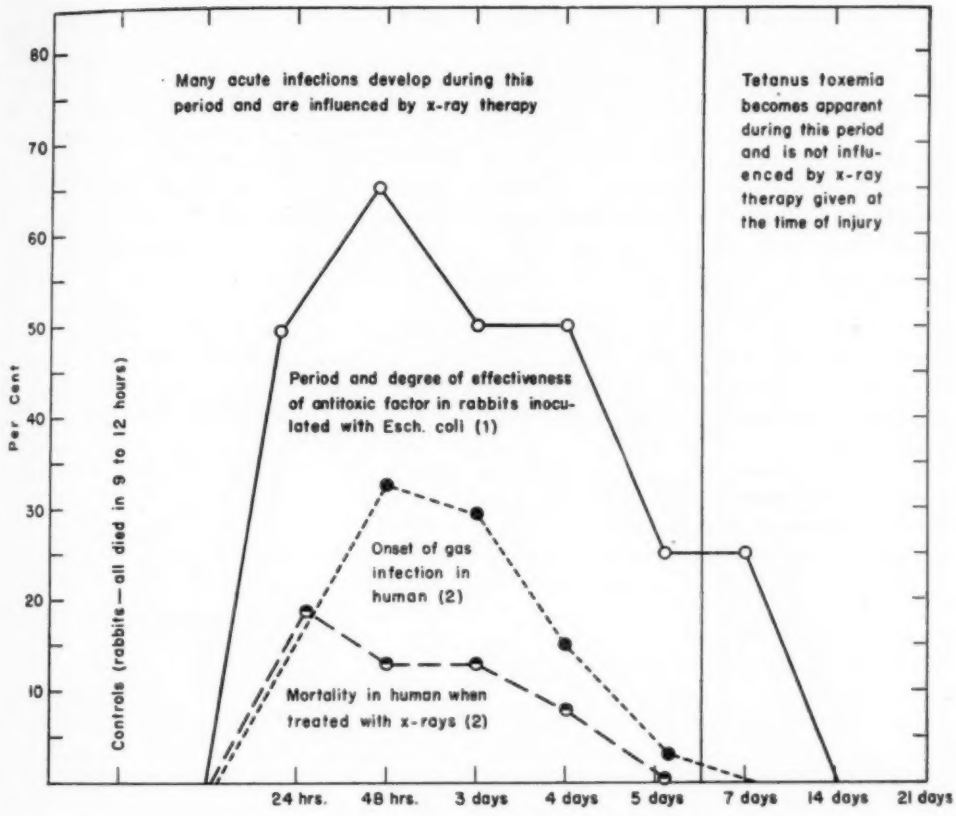

Fig. 1. From this composite graph, it is obvious that if x-rays for prophylaxis are given soon after the injury occurs, the period of protection begins in a few hours and continues for several days beyond the time a gas infection is likely to develop. Since the antitoxic factor is non-specific in character, it is also evident that the danger of infection from many other organisms is also eliminated or greatly minimized by irradiation.

(1) BISGARD, J. D., *et al.*: Radiology **39:** 691, December 1942.
(2) KELLY, J. F., AND DOWELL, D. A.: Radiology **37:** 421, October 1941.

All of these reports make a total of 450 (post-traumatic) cases, with 53 deaths, or a mortality rate of 11.8 per cent. There is a consistency in these reports, from widely separated sources, which, regardless of what happens in animals, establishes this study as a completed clinical experiment, and there is such a thing as a clinical experiment, in spite of any number of opinions to the contrary expressed by professional animal research workers.

Prophylaxis: The use of the x-rays in the prevention of gas gangrene and other types of wound infection has been previously advocated (15, 18, 20, 21, 22), and there is no reason at this time to modify our belief in the procedure. In fact, all experimental and clinical work supports it so strongly that it seems mandatory that radiation therapy be used for prevention of infection in contaminated wounds.

Finally, the works of Bisgard and Rigos bring out nothing to disprove our contention that x-ray therapy is effective in acute spreading peritonitis. We feel that many people are much better off producing their own antitoxin after radiation therapy than they would be in attempting to live after the peritoneal cavity has been assaulted by the application of various sulfa powders and crystals, which, at the best, are only bacteriostatic agents and not to be com-

pared in value with an effective antitoxin free of any confusing reactions or serious complications. Bisgard's work, proving the absence of any antitoxic action from the use of the sulfa drugs and Meleney's report (23, 24) on the work of the National Research Council Committee on Wound Infection, in which investigation it was shown that these drugs were ineffective in preventing wound infection, should leave little doubt as to which method to use. X-rays will bring about both of these results (prevent wound infection and produce an antitoxic factor) as well as hold unpleasant or dangerous reactions to the minimum.

Period of Immunity with Relation to Secondary Infection: The usual period of onset of infection with streptococci or the gas-forming group following injury is well covered by the period of immunity obtained from x-ray therapy (see Fig. 1), and our observations have led us to believe that any infection from the rapidly growing organisms will be prevented if x-rays are used for the first three days after injury. As a result of this effect, it appears that other more slowly growing organisms are not able to establish a growth; thus the so-called secondary infections, usually radioresistant, are also eliminated indirectly by this prompt effect of the x-rays on the early invaders.

Recovery of Tissues After Use of Specific Antitoxin: The effect of the specific antitoxin for diphtheria and the effect of the antitoxic substance formed in the tissues following radiation show no appreciable difference. Diphtheria antitoxin will prevent the onset of diphtheria, and there is considerable evidence in the literature that the use of the x-rays following an injury such as is commonly associated with a gas infection will prevent the onset of that complication.

It is also common knowledge that tissues badly involved in a well developed case of diphtheria show prompt improvement with a minimum of local destruction after administration of the antitoxin. A similar recovery of tissues is noted in gas gangrene after x-ray therapy; sometimes the recovery has been complete when the tissues seemed hopelessly diseased. *Those who assume that there is no known method for the prevention and the treatment of gas gangrene are in error. The most important fact, however, is that the x-rays will not only prevent gas gangrene, but will also prevent many other infections if used early.* Incidentally, and of some importance to the patient, when x-rays are used for the prevention or treatment of wound infection, it is not necessary to remove the involved tissues unless they are hopelessly destroyed. There is no justification for the removal of tissues under suspicion of involvement or only slightly involved, though it is a common surgical practice at this time.

The value of x-rays when they are used early for prevention of wound infection cannot be overemphasized. Specific antitoxins are the ideal means of preventing and treating infections, and, therefore, no measure could be more satisfactory from every angle than to have the patient produce his own antitoxin, which is non-specific in character and active at the time when the majority of infections from contamination are likely to appear. It is simple and safe to produce and costs little. The dangers from such application of the rays are less than the dangers associated with many other forms of prophylaxis or therapy. If there is a justifiable reason for not using x-rays for the prevention and treatment of wound infection, it has not been proved up to this time.

Tetanus: It seems probable that with a little study of the space factor and other technical details of administering the x-rays, tetanus may also be prevented, but at the present time reliance must be placed on tetanus antitoxin and it should be used in all instances.

Sulfonamides: The Only Recognized Contraindication: The ability of sulfonamides to alter or to inhibit the effect of x-rays is apparent from both clinical and experimental observations (25–32), and the attempt to combine the sulfa drugs and x-rays to produce a beneficial effect is to be

thoroughly condemned. Any attempt to judge the effect of either agent when they are combined is also to be condemned. The mortality may not be increased to any great extent, but the morbidity, as shown by increased number of necessary amputations, is definitely high, and more x-ray therapy will be required to secure even a fair result in cases where small doses and lower kilovoltages would suffice if the drug were omitted.

Penicillin: Since penicillin is a biological product, there is no contraindication to its use with x-ray therapy. Why penicillin is so often referred to as a chemotherapeutic agent is not clear.

SUMMARY

A review of the experimental work on the effect of roentgen rays in infections over the past forty years reveals certain findings with such consistency as to establish them as facts. A review of clinical reports over the same period reveals certain observations which are in agreement with the experimental findings with such consistency as to establish the same facts. From these facts, based on experimental and clinical proof, the following conclusions seem indicated.

The use of x-rays for prevention and treatment of certain acute infections requires the presence of three essential factors: (*a*) the dosage factor, (*b*) the tissue factor, and (*c*) the time factor. When these factors are present, a non-specific antitoxic substance is created in the tissues after a few hours which is effective for several days.

From the foregoing experimental and clinical data, a law of roentgen irradiation effect on certain pathogenic organisms may be postulated as follows:

When an area of living tissue receives an adequate dose of roentgen radiation, non-specific antibodies are liberated after a period of some hours which, depending on the time of irradiation, will either prevent or cure certain infections having a short incubation period, provided no chemical agents are used simultaneously which inhibit or alter the effect of the rays.

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Radiological Use of Fast Protons

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EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in large part, been due to the very short penetration in tissue of protons, deuterons, and alpha particles from present accelerators. Higher-energy machines are now under construction, however, and the ions from them will in general be energetic encugh to have a range in tissue comparable to body dimensions. It must have occurred to many people that the particles themselves now become of considerable therapeutic interest. The object of this paper is to acquaint medical and biological workers with some of the physical properties and possibilities of such rays.

To be as simple as possible, let us consider only high-energy protons: later we can generalize to other particles. The accelerators now being constructed or planned will yield protons of energies above 125 Mev (million electron volts) and perhaps as high as 400 Mev. The range of a 125 Mev proton in tissue is 12 cm., while that of a 200 Mev proton is 27 cm. It is clear that such protons can penetrate to any part of the body.

The proton proceeds through the tissue in very nearly a straight line, and the tissue is ionized at the expense of the energy of the proton until the proton is stopped. The dosage is proportional to the ionization per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate intensely a strictly localized region within the body, with but little skin dose. It will be easy to produce well collimated narrow beams of fast protons, and since the range of the beam is easily controllable, precision exposure of well defined small volumes within the body will soon be feasible.

Let us examine the properties of fast protons somewhat more quantitatively. Perhaps the most important biological quantity is the specific ionization, or number of ions per centimeter of track. This quantity is not difficult to calculate. The results of such calculations are shown in Figure 1, where the range of protons in tissue is plotted for protons of various energies. In the same figure, the specific ionization is plotted as a function of the range in tissue. For purposes of calculation, tissue has been assumed to have the molecular formula (1): $C_{0.5}H_8O_{3.8}N_{0.14}$, and to be of unit density, *i.e.*, 15 per cent protein and 85 per cent water. The calculations can be easily extended to other materials and densities.[2] The accuracy is perhaps 5 per cent. However, exact values for various tissues can be quickly measured as soon as the fast protons are available.

Figure 1 shows, for example, that if we want to expose a region located 10 cm. be-

[1] Accepted for publication in July 1946.

[2] The range of a proton in air in meters is given by the convenient formula $R = (E/9.29)^{1.8}$ where the energy is expressed in Mev. The range in tissue is 1.11×10^{-3} times the range in air. The stopping power of other substances may be found in Livingston and Bethe: Rev. Mod. Physics **9**: 246, 1937. The physical calculations of this paper will be submitted to the *Physical Review* for publication.

low the nearest surface, it will be necessary to have protons of 115 Mev. If a depth of 15 cm. were required, then 140 Mev protons would be needed. The specific ionization curve needs a little interpretation. If we interpret the abscissae as the residual range, then there should be little difficulty in visualizing the specific ionization at various depths within the body. As a particular example, let us consider 140 Mev protons. In Figure 2, the dotted line is a depth-dose curve obtained by plotting the specific ionization taken from curve II of Figure 1 against the depth of proton in the tissue. Thus, at the surface, the residual range is 15 cm., and curve II of Figure 1 shows that the specific ionization for a proton of 15 cm. range is 0.15 million ion pairs per centimeter. This point has been adjusted to 100 per cent in Figure 2. When the proton has proceeded into the tissue 7 cm., its residual range is 8 cm. and the ionization of a proton of 8 cm. range is 0.2 million ion pairs per centimeter or 133 per cent of the surface dose. The rest of the curve can be obtained in the same way, and we see that the curve rises sharply in the last few centimeters. The average ionization over the last centimeter is about six times that at the surface. In the final half centimeter of a particular proton track, the average dose is sixteen times the skin dose. The full curve is perhaps more realistic, however, and it will be explained later.

It is well known (2) that the biological damage depends not only on the number of ions produced in a cell, but also upon the density of ionization. Thus the biological effects near the end of the range will be considerably enhanced due to greater specific ionization, the degree of enhancement depending critically upon the type of cell irradiated.

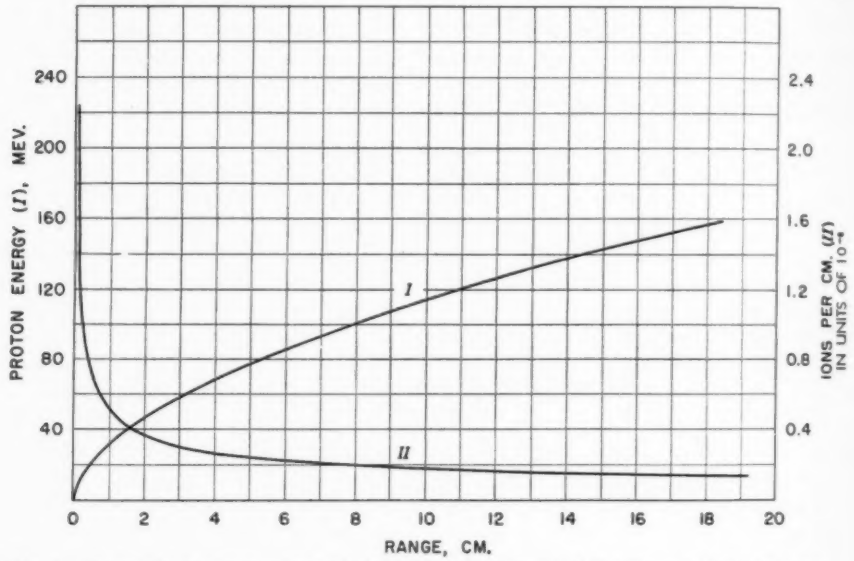

Fig. 1. Curve I is the range-energy relation in tissue. Curve II shows the specific ionization as a function of the residual range of a proton in tissue.

At this time we might inquire about the current of protons required for an irradiation. I shall use the roentgen equivalent dose, as it particularly is amenable to calculation for this application. One roentgen equivalent dose (r.e.d.) of protons will have been received at a certain point in the tissue when 83 ergs of energy have been absorbed per gram of tissue. In the last centimeter of range a proton loses 30.1 Mev (energy of a proton of 1.0 cm. range; see curve I of Figure 1). Since 1 Mev is equal to 1.6

millionths of an erg, each proton loses 48 millionths of an erg in the last centimeter. Hence, to produce 1 r.e.d. averaged over the last centimeter of depth requires $83/48 \times 10^6 = 1.72$ million protons per square centimeter. To produce 1,000 r.e.d. will require 1.72 billion protons per square centimeter. This corresponds to a current of 2.75×10^{-10} amp./cm.[2] of protons for a one-second exposure or 4.6×10^{-13} amp./cm.[2] for a ten-minute exposure.[3] The machines now under construction should have little difficulty in producing such currents. In fact, it is expected that they will yield currents millions of times as great. It will be simple to collimate proton beams to less than 1.0 mm. diameter or to expand them to cover any area uniformly.

Let us now become a little more technical and consider secondary effects. First, the energy loss of the proton is a statistical effect due essentially to the production of ions along its path; hence, not all protons of the same energy will stop at the same distance beneath the skin. This effect is called range straggling and is easy to calculate. The results of such calculations can be summarized by saying that the longitudinal width in which most protons come to rest is about 1 per cent of the initial range.[4] The effect of this on the depth dose curve is qualitatively shown in Figure 2. As a result of straggling, the full curve obtains instead of the dotted one.

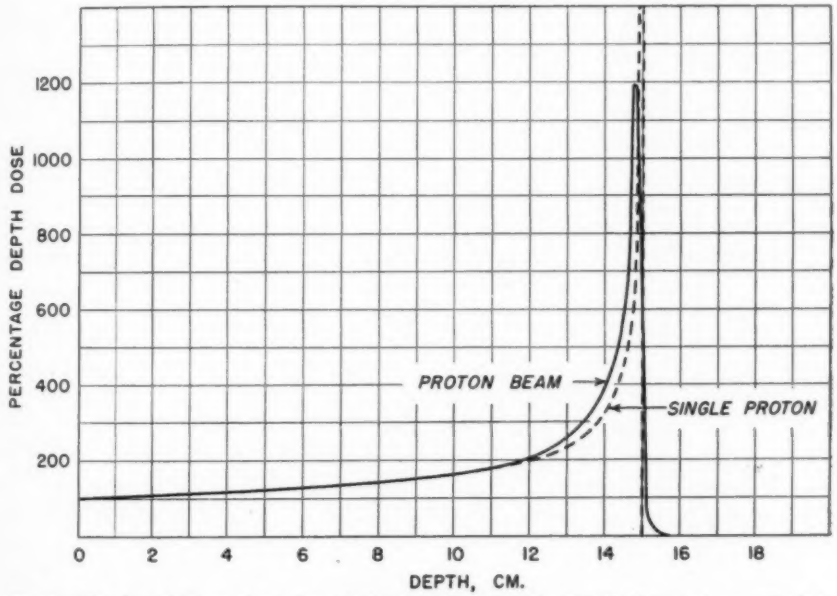

Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.

A second effect is due to the many small

[3] More generally the r.e.d. at a point x cm. below the surface is given approximately by the formula

$$\text{r.e.d.} = 4.8 \times 10^{10} \frac{jt}{(R - X)^{0.444}}$$

where R is the total range of the proton in tissue in cm., j the current density or protons in amperes/cm.[2], and t the exposure time in seconds. The formula is not accurate in the last millimeters of range.

[4] The protons come to rest so that the distribution of their end-points is given by $P(x)dx = \frac{R}{\alpha\sqrt{\pi}} e^{-\frac{(R-x)^2}{R^2\alpha^2}} dx$, where x is the distance below the surface, and α is given by

$$\alpha = \frac{7.1}{E_0^{1/2}} \left(\frac{NZz^2R}{E_0}\right)^{-0.055}$$

where N is the atoms per cm.[3], Z is the atomic number, z is the ion charge number, E_0 is the rest energy of the ion in Mev, and R is the range in cm.

angle scatterings of the proton as it passes the nuclei of the atoms of the tissue. This is called multiple scattering, and its effect is to spread the end of the beam out transversely. It is also easy to calculate, and it turns out that the transverse width which an infinitely narrow starting beam would have at the end of its range is about 5 per cent of the initial range.[5] Both effects are small, but they do indicate the limitations of precision available.

A third effect is that due to the nuclear absorption and scattering of the protons. The exact behavior of protons in nuclear reactions at such high energies as considered here must be determined by experiments to be carried out in the future. Present experiments using high-energy neutrons give good estimates of the radii of most nuclei (3). Probably whenever a fast proton hits the nucleus it will be captured and its energy will appear in several slower protons, alpha particles, or neutrons. In any case, the probability of a proton impinging on a nucleus after traveling 10 cm. in tissue will be about 25 per cent. The effect tends to decrease the specific ionization at the end of the range by 15 to 30 per cent. Inasmuch as the specific ionization is several times greater at the end of the range than it is at the beginning, this will not be serious.

A similar effect is that due to elastic scattering of the protons by nuclei. The probability of this type of scattering is essentially the same as that of absorption. In this case, however, the proton is not stopped but continues at the same energy but in a different direction. The effect, then, is to diffuse about 20 to 40 per cent of the beam. For fairly broad beams this would not be noticeable because such scattering will be predominantly forward.

The above should be the principal effects, and we see that our original picture of a proton beam proceeding without spreading until it is stopped at high-specific ionization in the tissue is only slightly modified. It will be possible to treat a volume as small as 1.0 c.c. anywhere in the body and to give that volume several times the dose of any of the neighboring tissue. The exact behavior of protons of the energy considered here will become known only when such protons are available for experiment.

In treating large tumors, for example, one will want to cover the whole volume with the very high ionization density which obtains over the last few millimeters. This can easily be accomplished by interposing a rotating wheel of variable thickness, corresponding to the tumor thickness, between the source and the patient.

The exposure can be monitored precisely simply by placing a shallow ionization chamber between source and patient. Absolute determinations of the dosage can be determined by measuring ionization currents in gases of the elements of tissue or in a gas which mocks up the molecular formula of tissue. What makes the problem of dosage measurement so simple is the absence of the wall effects encountered in x-ray or neutron exposure measurements. This is because the high-energy proton produces its secondary electrons at such low energy that their range is essentially zero.

The above results are easily generalized to other particles. Range and specific ionization of deuterons or alpha particles can be determined from Figure 1 for protons. If the proton energy ordinates are multiplied by two, as well as the range, curve 1 then holds for deuterons. Thus a 200 Mev deuteron has 16 cm. range. The specific ionization remains the same, however, and a deuteron of 16 cm. range makes 0.14×10^6 ion pairs per cm. For alpha particles both ordinates are multiplied by four, but the range is left un-

[5] The transverse distribution of the end-points of the protons is given by

$$P(y)dy = \frac{R}{\beta\sqrt{\pi}}\, e^{-\frac{y^2}{R^2\beta^2}}\, dy$$

where y is the distance from the average end of the range measured perpendicular to the initial direction of the beam and β is given by

$$\beta = 12\left(\frac{Z}{E_0}\right)^{1/2}\left(\frac{NRZ^2}{E_0}\right)^{-0.055}$$

The numerical constant should be determined more accurately by experiment.

changed. Thus a 400 Mev alpha particle has a range of only 8 cm., but its specific ionization is 0.8×10^6, four times as great as for a proton of the same range. The intense specific ionization of alpha particles, when considered in the light of Zirkle's results, will probably make them the most desirable therapeutically when such large alpha particle energies are attained. For a given range, the straggling and the angular spread of alpha particles will be one-half as much as for protons. Heavier nuclei, such as very energetic carbon atoms, may eventually become therapeutically practical.

One naturally asks what are the advantages of fast protons over high-energy electrons such as those from a betatron (4). This question can be answered only by medical workers, and the answers will probably be different for different kinds and sizes of tumors. Certainly the differences between fast electrons and protons are only quantitative. The specific ionization for protons is much greater, and the concentration of ionization in a given volume is also greater because the straggling and spreading of electrons is worse. On the other hand, electrons of sufficient energy can be produced by more modest equipment.

Finally, I would like to emphasize the danger which will be lurking near the proposed high-energy machines. We have seen that a current density of a few times 10^{-10} amp./cm.^{2} for one second could have lethal effects. The particles can penetrate the metal walls of the machines, and if less than one billionth of the proposed currents of about one microampere is scattered in the wrong direction, then workers may be in danger. This becomes particularly apparent when one considers that the range in air of a 150 Mev proton is about 150 meters. On the other hand, the range of such a proton in lead is only a few inches, and with thoughtful precaution accidents can be averted.

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Measurement of Radioactive Phosphorus in Breast Tumors in Situ; a Possible Diagnostic Procedure

Preliminary Report[1]

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RADIOACTIVE phosphorus administered orally or intravenously in the form of disodium hydrogen phosphate solution is assimilated by different tissues in varying degrees. The concentration in tissues at any given time after administration depends on the metabolic activity of constituent cells. In general, malignant growths have a higher metabolic rate than the tissues from which they originate, and regenerating tissues also show greater metabolic activity than normal tissues. In both types of growth, therefore, a greater amount of phosphorus is taken up for the new cells that are forming. The differential distribution can be determined quantitatively by measuring the radioactivity of ashed samples of the tissues by means of a beta-ray electroscope, an electrometer, or by a Geiger-Müller counter. Such a determination necessitates the removal of the tissues in part or in whole.

If a lesion is located in the skin or close beneath the skin, the beta rays emanating from the disintegrating phosphorus atoms localized in the lesion should penetrate the tissues and come through into the air in sufficient number to be readily detected by a Geiger-Müller counter placed on the skin. Marinelli (1), in 1942, reported measuring such rays with a Geiger-Müller counter on three patients, one with a melanoma and two with mycosis fungoides. One of the present writers (Low-Beer), using a similar method, found increased activity not only over such skin lesions as mycosis fungoides, squamous-cell and ulcerating basal-cell carcinomata, psoriasis, eczema, and cutaneous Hodgkin's disease, but also over subcutaneous lesions, such as lymphosarcoma in lymph nodes, cervical node metastases from transitional-cell carcinoma of the nasopharynx, bone metastases in the skull from carcinoma of the lungs, and others.

These findings suggested the investigation of the uptake of radioactive phosphorus in human breast tumors in order to determine, first, whether the differential concentration of phosphorus in such tumors could be detected by surface measurements, and second, whether or not it would be feasible to distinguish preoperatively between benign and malignant breast tumors by such surface measurements. It was thought that the same method might indicate the presence or absence of metastatic lesions in the axilla or supraclavicular area. To determine these points we studied patients with breast tumors prior to surgery. The measurements were made with bell-jar type Geiger-Müller counters with thin glass windows having a diameter of 1.5 to 2.5 cm.

Each patient was given from 300 to 500 microcuries of radioactive phosphorus intravenously in the form of isotonic disodium hydrogen phosphate solution, twenty-four or forty-eight hours before operation. Two, four, six, and twenty-four hours following injection, surface measurements were made directly over the palpable breast tumor and over comparable areas on the opposite normal breast and other fleshy parts of the body. After surgical removal, samples of the tumor, skin, fat, normal breast tissue, and muscle were dissected, weighed, and ashed. The radio-

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activity of the ashed samples was determined quantitatively.

To date 25 patients have been so studied. Five of these had lesions that were obviously malignant at the time of clinical examinations, and this was confirmed in the laboratory. In all 5 patients the counts over the palpable tumor were higher by at least 25 per cent than in corresponding areas of the opposite breast and adjacent areas of the same breast.

Twenty patients had palpable tumors in which the question of malignancy could not be resolved clinically. Eleven of these patients showed at least 25 per cent higher counts over the tumor area than over other areas in the same breast or corresponding areas of the opposite breast. All of these 11 patients were later proved by microscopic examination to have malignant tumors. Nine patients showed less than 25 per cent difference in counts between the involved areas and adjacent areas in the same breast and corresponding areas on the opposite breast. Of these 9, 8 were found by microscopic examination to have benign tumors. One of the group was shown by microscopic examination to have a malignant tumor. It was, however, a mucoid carcinoma with relatively few cells.

Postoperatively, quantitative determinations of the radioactivity of the removed tissues showed a five to ten times greater uptake of radioactive phosphorus in the cancer tissue than in any of the other tissue examined. The mucoid cancer was the only exception, its radioactive phosphorus content being the same as that of the normal breast tissue. In the tumors shown to be non-malignant, the differential uptake of radioactive phosphorus demonstrated by the assay method never exceeded twice that in normal breast tissue.

The findings to date indicate that breast cancers can probably be diagnosed by this method, except for such slow-growing ones as mucoid carcinoma and, we expect, very deep-seated ones. The results appear to be sufficiently suggestive to justify further investigation. Until such time as this method of diagnosis may be established on a broader statistical line, it is suggested that a decision for or against the use of surgery in doubtful cases of malignancy of breast tumors should not be influenced by these findings.

It must be emphasized that this study is concerned solely with the *diagnosis* of carcinoma of the breast. The amount of radioactive material used would not "treat" the lesion at all.

Similar procedures are being used in an attempt to determine whether palpable axillary and supraclavicular nodes contain metastases or whether non-palpable metastases are present, but the results to date do not justify publication.

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A Clinical Study of Normal and Pathologic Motor Activity of the Gallbladder

Preliminary Report[1]

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FROM TIME TO time we have observed that patients were subjected to cholecystectomy merely because they presented right upper abdominal complaints and roentgen evidence of delayed emptying of the gallbladder (so-called poorly functioning gallbladder without stones), though general examination revealed no demonstrable cause for their symptoms. In most instances, the symptoms were unrelieved and histologically the gallbladders proved to be normal. This condition prevails despite the fact that many observers, as Graham and Mackey (1), Ivy and Bergh (2), Ravdin, Riegel, Johnston, and Morrison (3), Sosman (4), and others, have emphasized the differential diagnosis between the surgical and the non-surgical gallbladder. While lack of this knowledge may be one of the factors accounting for such errors in surgical judgment, another more important cause is the lack of completely established concepts concerning the normal physiology of the biliary tract.

With these considerations in mind, we decided to direct our investigation to one phase of biliary tract physiology, namely, the motor activity of the gallbladder.[2] Since we employed the x-ray method for this study, our interest was mainly centered on the mechanism of emptying of the gallbladder.

Before continuing with this discussion, it is necessary to clarify our conception of the term stasis, since it is generally associated with any consideration of this subject. To avoid any misconceptions, from the roentgen standpoint, we understand stasis to mean simply delayed emptying of the gallbladder. Further, for the time being, we are not concerned with the maze of theories (6, 7, 8*a*, 9) anatomic and physiologic, which have been offered in an attempt to explain the cause of delayed emptying, but merely with its actual demonstration.

In studying the literature, one finds reports of experiments and observations on animals which have been subjected to various operative procedures (5, 10). Unquestionably, these procedures alter the normal functions of the gallbladder. Furthermore, in view of the fact that animals do not present the same conditions as man, either as to the anatomy and physiology of the gallbladder or the chemistry of the bile, the direct clinical application of such observations is a fallacy.

Graham and Cole's important discovery of visualization of the gallbladder (11) lends itself ideally to an investigation of this subject in man. Their method has been thoroughly studied by Boyden (8*b*), who employed a specific meal (five egg yolks, well mixed with a half a pint of cream) to determine the emptying time of the gallbladder. This highly concentrated fatty meal has been utilized by many investigators to study motility of the gallbladder and has been generally adopted as a routine procedure. In addition, other investigators (12, 13) have reported on delayed gallbladder emptying following starvation and high carbohydrate diets. All of these methods, while of great scientific interest, fail to conform with the normal daily routine dietary habits of the individual.

We have therefore decided to reopen the

[1] From the Departments of Radiology and Pathology, Menorah Hospital, Kansas City, Mo. Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

[2] According to Ivy (5), the physiology of the gallbladder is manifested in three types of activity: absorption, secretion, and motor activity.

subject and study the motility of the gallbladder by a method which is in conformity with normal eating habits.[3] This new approach may give additional information concerning the motor activity of the gallbladder under normal and pathologic conditions. It may seem trite to state that basic knowledge of the normal must be established before determining the pathologic, but, in retrospect, we fear this process has been reversed in roentgen observations of the gallbladder.

Our method of study to determine the normal is as follows: (1) From the outpatient clinics, individuals of different ages, sex, and nationality are selected, with no history, past or present, of abdominal complaints. (2) On the day preceding the roentgen examination, the patient is instructed to abstain from all fatty foods at lunch. (3) At 4 P.M., 3.6 gm. of sodium tetraiodophenolphthalein[4] is taken in water or grape juice, and this dose is repeated at 6 P.M. if the subject is overweight. This dye is employed because our past experience is mainly based on its use and most of the physiologic experiments have been performed with it. No food is eaten until the x-ray examination the following morning at 8 o'clock. (4) The patient is then instructed to eat his usual breakfast and, one hour later, x-ray studies are again made. (5) Further roentgen studies are made one hour after each subsequent routine meal until the dye disappears. In the meantime, the patient pursues his daily routine.

The findings according to this method are recorded in the accompanying table.

Before discussing the data in the table and our plan of further investigation, we wish to state that we are fully aware that definite conclusions cannot be drawn from this small series of observations. The great shortage of films during the past war years has been a serious handicap and is mainly responsible for this shortcoming. Certain trends, however, seem apparent.

There is a wide range of normal emptying rate within the first twenty-four hours, having no definite relation to age, sex, or eating habits. In only one case, Case 11, were forty-eight hours required for complete emptying of the gallbladder, even though meals ample in fat were consumed. In contrast, a sixty-six-year-old man, Case 9, showed complete emptying after a breakfast which contained practically no fat. Two patients, Cases 8 and 12, showed no contraction of the gallbladder after a breakfast containing an appreciable amount of fat, but emptying occurred after subsequent meals variable in fat. A similar response was noted in Case 4, where meals of moderate fat content were consumed.

These facts, meager as they are, suggest future trends of our investigation. Normal subjects showing poor contraction after their routine meals will be further investigated with the Boyden meal. It is possible that a person may show good emptying with the Boyden meal, yet may reveal marked delay under his normal eating habits. On the other hand, there may be delayed response after the Boyden meal in someone who is accustomed to consuming large quantities of fat. In other words, we are bent on determining whether the response to the Boyden meal is a true test of the emptying time of the gallbladder for a particular individual.

Further, it is essential to determine the degree of variability of the individual emptying rate under normal conditions. Returning to Case 11, in which forty-eight hours were required to empty the gallbladder completely, we must consider that this patient presented no abdominal complaint. In this respect, she was as normal as those with complete emptying within the first twenty-four hours. And it may very well be that in our future studies, comprising a large series, we will find individuals who require more than forty-eight hours for emptying of the gallbladders, but who still may be perfectly normal. If this be the case, then we must revise our ideas concerning delayed emptying of the gallbladder (so-called poorly

[3] In future studies, in addition to recording the contents of the meal, we intend to express the amount of fat consumed by actual figures.

[4] We intend to conduct a comparative series of studies using Priodax.

TABLE I: RATE OF GALLBLADDER EMPTYING IN NORMAL SUBJECTS FOLLOWING THEIR USUAL ROUTINE MEALS

Subject Sex Age Height Weight	Concentration 15 Hours After Ingestion of Dye	Breakfast	Approximate Contraction 1 Hour After Breakfast, %	Lunch	Approximate Contraction 1 Hour After Lunch, %	Dinner	Approximate Contraction 1 Hour After Dinner, %	Breakfast	Approximate Contraction 1 Hour After Breakfast, %
1. E. H. F 55 5′ 2″ 92 lb.	Good	1 piece buttered toast, 2 scrambled eggs, 1 cup black coffee	50	1 ham salad sandwich, 1 cup coffee with cream, apple	75	Macaroni and cheese, bread pudding, lemonade	Empty		
2. E. W. F 59 5′ 4″ 221 lb.	Good	6 crackers, 2 cups coffee with cream	50	Boiled cabbage, boiled beef, lunch meat, sliced tomatoes, 1 cup coffee with cream	75	Fried corn, sliced tomatoes, lima beans, bacon, bread and butter, coffee	95		
3. C. H. M 41 5′ 9″ 128 lb.	Fair	Cream of wheat with milk, 1 slice bread and butter, 1 cup coffee with milk	60	2 frankfurters, spinach with butter, 2 slices bread and butter, iced tea, canned peaches	75	Steak, boiled potatoes, gravy, buttered peas, 2 slices bread and butter, cinnamon roll, 1 glass milk	Empty		
4. L. S. F 70 5′ 3″ 188 lb.	Good	2 slices buttered toast with jelly	No contraction	1 hamburger patty, 2 slices bread and butter, 1 cup coffee with cream	Empty				
5. R. J. M 24 6′ 1″ 210 lb.	Good	Wheaties with cream, 2 soft-boiled eggs, 2 pieces toast with oleo, 1 glass milk, 2 glasses water, 1/2 cantaloupe	90	2 pork chops, mashed potatoes, 1 slice bread and oleo, 2 glasses milk	Empty				
6. C. deL. F 14 5′ 3″ 109 lb.	Good	2 slices buttered toast, 1/2 scrambled egg, 1 glass milk, 1 cup coffee with cream	75	1 frankfurter, 2 glasses malted milk, nut and chocolate candy bar, ice cream cone	Empty				
7. T. deL. F 16 5′ 2″ 109 lb.	Good	2 slices buttered toast, 1/2 scrambled egg, 1 glass milk, 1 cup coffee with cream	75	1 frankfurter, 2 glasses malted milk, nut and chocolate candy bar, ice cream cone	Empty				

8. B. B. F 14 5′ 2½″ 150 lb.	Medium	2 fried eggs, 2 slices bread, no butter, 1 tomato	No contraction	1 frankfurter, 2 glasses buttermilk, 1 bottle coca cola	Empty				
9. T. B. M 66 5′ 9½″ 133 lb.	Good	Sliced oranges, dry toast, cup cake, 1 cup coffee with cream	Empty						
10. B. H. F 33 5′ 1″ 131 lb.	Good	1 scrambled egg, buttered toast, coffee	85	1 ham salad sandwich, coffee, potato salad, coca cola	Empty				
11. H. H. F 54 5′ 4″ 151 lb.	Good	2 scrambled eggs, 1 piece buttered toast, 1 cup coffee	50	1 ham salad sandwich, combination salad, 2 cups coffee	75	Chicken steak, buttered carrots, 2 slices bread with butter, 1 glass grapejuice	Still faintly outlined	2 pieces buttered toast, 1 cup coffee	Still faintly outlined*
12. I. W. F 31 4′ 11″ 199 lb.	Good	2 scrambled eggs, 2 pieces buttered toast, 1 cup coffee with cream	No contraction	2 sausages, 2 fried eggs, fried potatoes, 1 slice bread, 1 glass buttermilk, 1 coca cola	25	2 fried eggs, 2 slices bacon, 2 pieces bread, 1 tomato, 1 plum, 2 glasses water	Empty		
13. J. M. F 29 5′ 1″ 120 lb.	Good	1 scrambled egg, 2 pieces toast, 1 glass milk, 1 cup coffee with cream	No record						
14. C. S. M 57 5′ 9″ 172 lb.	Fair	2 scrambled eggs, buttered toast, 1 glass milk	25	Roast beef, corn, potatoes	Empty				
15. W. K. M 25 5′ 10″ 144 lb.	Good	Scrambled eggs, toast, coffee	75	Oatmeal, milk	Empty				
16. L. G. F 35 5′ 2″ 127 lb.	Good	2 strips bacon, 2 eggs, ⅓ grapefruit, 2 slices raisin bread toast, butter, jelly, 1 cup black coffee	25	Grilled cheese sandwich, small coca cola, ice cream	50	4 rich cookies, 2 cups tea, ½ slice bread, 2 pats butter, 1 cup ice cream	80	Oatmeal with milk, 2 slices whole wheat bread with butter and jelly, orange, 1 cup coffee with milk	Empty

* Approximately one hour after lunch (steak, corn on cob with butter, 1 slice of bread and butter) emptying was complete.

Table cont. on p. 498)

TABLE I: RATE OF GALLBLADDER EMPTYING IN NORMAL SUBJECTS FOLLOWING THEIR USUAL ROUTINE MEALS (*Continued*)

Subject Sex Age Height Weight	Concentration 15 Hours After Ingestion of Dye	Breakfast	Approximate Contraction 1 Hour After Breakfast, %	Lunch	Approximate Contraction 1 Hour After Lunch, %	Dinner	Approximate Contraction 1 Hour After Dinner, %	Breakfast	Approximate Contraction 1 Hour After Breakfast, %
17. P. S. F 30 6′ 3½″ 189 lb.	Good	1 egg, 2 strips bacon, 1 slice buttered toast, jelly, 1 cup coffee, 1 teaspoon cream	50	½ cup cottage cheese, 1 small raw carrot, 1 slice bread, 1 teaspoon butter, 1 cup coffee, 1 teaspoon cream	80	½ lunch ham sandwich, 1 scant cup potato chips	No change	1 piece buttered toast, 1 cup black coffee	Empty
18. H. M. F 40 5′ 3″ 113½ lb.	Good	2 strips bacon, 2 eggs, 2 slices raisin bread toast, butter and jelly, ½ grapefruit, 1 cup black coffee	50	1 grilled cheese sandwich, 1 cup coffee	75	5 rich cookies, 1½ cup tea, ½ slice bread, 1 pat butter, ½ cup cream	Empty		
19. B. N. F 41 5′ 3″ 165 lb.	Good	2 pieces toast, 1 cup black coffee, 1 glass orange juice	Practically no contraction	Combination salad, baked trout, mashed potatoes and gravy, corn bread, peach pie, 1 cup black coffee	25	1 boiled frankfurter, fried potato cake, 1 cup green beans, 2 small pieces celery, sliced peaches, 1 slice bread, 1 cup tea, cookie	50	1 piece toast, small glass pineapple juice, 1 cup black coffee	Empty
20. M. S.† F 36 5′ 1″ 136 lb.	Practically no concentration on repeated administration of dye								
21. B. C.† M 27 5′ 9″ 228 lb.	Practically no concentration on repeated administration of dye								

† The failure of visualization of the gallbladder may be due to premature contractions, according to Boyden (8*c*).

functioning gallbladder) and stasis. May not our present concept of stasis of the gallbladder be subject to the same errors as our concept of stasis of the colon entertained in a bygone era? It will be recalled, as Barclay (14) points out, that "it was thought that in the alimentary tract, movements took place on a fixed schedule—if this schedule was not adhered to, stasis occured in various parts, toxic products were absorbed, and symptoms would result. The diagnosis of stasis was invoked for seemingly any and every disease. Stasis-minded surgeons were prone to perform the slinging-up operations on the caecum." Are we passing through a similar phase in relation to the gallbladder?

Our future studies will be directed toward answering these questions and determining the validity of the above concepts. Finally, our efforts will be directed toward taking the problem of delayed emptying of the gallbladder out of the realm of empirical speculation and placing it on a scientific basis.

SUMMARY

1. A preliminary report is made on a study of one phase of biliary tract physiology—the motor activity of the gallbladder. Since the x-ray method is used, interest is mainly centered on the mechanism of emptying.

2. To determine the normal emptying time of the gallbladder, a method is employed which conforms with the normal eating habits of the individual.

3. Present and future trends of this investigation are discussed.

4. A concept concerning delayed emptying of the gallbladder (so-called poorly functioning gallbladder), or stasis, is presented.

NOTE: We wish to thank Mrs. Mildred Kice and Miss Helen Root for aid in preparation of the manuscript.

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Liposarcoma: A Case Report[1]

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IT IS remarkable that a tissue so common as fat and so prone to benign tumor formation should so seldom be the source of cancer. Liposarcomas, while not often omitted from any classification of tumors, occur only rarely. Although the tumor was recognized histologically by Virchow in 1857, it is difficult, from available data, to estimate the number of cases reported. In a critical analysis of the literature in 1916, Robertson (10) accepted only 18 cases. Moreland and McNamara (8) comment upon the few recorded instances but suggest that these growths may have been mistaken for endotheliomas and other tumors. They describe 9 cases of liposarcoma in a group of 16,000 patients with tumors, and offer the opinion that the clinical frequency may be greater than the few reported histories would indicate. Mallory (7), on the other hand, says that the pathological diagnosis of liposarcoma is unusual, that the presence of fat in tumor cells is not particularly uncommon and may merely indicate a degenerative phenomenon, and that he is rarely confident in making a diagnosis of liposarcoma. Stout (13), recently reporting upon a series of patients with liposarcoma, has comprehensively reviewed the literature and histology of these growths and compiled an extensive bibliography. He states that 134 cases are recorded, and adds 41 more which have been studied in the Laboratory of Surgical Pathology of Columbia University during thirty-seven years (21 originating from the Presbyterian Hospital, the remainder from other sources).

In the Columbia University group, 35 per cent of the tumors arose from the thigh, popliteal space, and gluteal regions; 16 per cent occurred in the retroperitoneal, perirenal, omental, and mesenteric tissues; 6 cases involved the trunk; 5 the head, face, and neck; 3 the groin and inguinal canal; 3 the leg; 3 the arm and forearm; 1 the breast. This distribution corresponds to that found by Moreland and McNamara and other authors, who place the most frequent site of origin in the soft tissues of the lower extremities or retroperitoneal space. Cases are reported occurring in the vulva (14), bone (12), extradural space (3), mediastinum (9), pleural cavity (2), uterus (11), and stomach (1).

The tumor may appear in patients of any age, including children (6), but is most often seen in the years between thirty and sixty. Unlike lipomas, which are said to be three times more common in females than in males, liposarcomas have been recorded slightly more frequently in the male sex. Growth, frequently rapid, may be slow and symptomless over a period of many years. The tumor is characteristically encapsulated, and seemingly readily removable, but recurs, often repeatedly and in a more anaplastic state, ultimately to cause death by pulmonary metastasis.

The theory, held for many years, that fat cells are merely fibroblasts modified for the function of fat storage is no longer acceptable. Fat cells are now believed to originate from their own specialized lipoblasts, which are readily distinguishable from fibroblasts, especially, according to Stout, when grown *in vitro*. Abnormal tumor growth of these lipoblasts usually brings about the development of a lipoma, more rarely a liposarcoma. While the majority of liposarcomas originate as such, an undetermined but definitely small percentage result from malignant change in an already existing lipoma.

Considerable variation of opinion exists as to the advisability of subdividing lipo-

[1] From the Neoplastic Service, Metropolitan General Hospital, Windsor, Ont. Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

sarcomas into several types, but for the present purpose it will suffice to follow Stout's suggestion that they be looked upon as a single group capable of manifesting different degrees of differentiation. He lists the following: (1) a well differentiated myxoid type; (2) a poorly differentiated myxoid type; (3) a round-cell or adenoid type; (4) a mixed group. It is questionable if cases of the first type ever metastasize, and by many authors they would not be accepted as sarcomas; the other types are definitely malignant.

Difference of opinion also prevails as regards the radiosensitivity of these tumors. Very few instances are recorded in which radiation in adequate dosage has been employed in their management, and brief and incomplete periods of follow-up examination detract considerably from the value of many of these accounts.

The case here reported was encountered in a series of more than 2,200 personally treated cancer patients. There is no other recorded instance of this disease in the pathological laboratories of the three general hospitals in the city of Windsor. The histologic diagnosis, made by Dr. S. M. Asselstine, has been confirmed by Professor James Miller of the Department of Pathology of Queen's University, Kingston, Dr. M. E. Maun of Wayne University Medical School, Detroit, and Dr. Arthur Purdy Stout of Columbia University, New York. Dr. Stout reported as follows: "I am in agreement with Dr. Asselstine that it is a liposarcoma. The tumor, both in its primary manifestation and in the lung metastasis, tends to form rounded cells, most of them with foamy cytoplasm, although some show no evidence of intracellular lipoid. This is, then, one of the less common round-cell forms of liposarcoma, which reproduce in their growth the appearance of brown fat. It is interesting to find a tumor which maintains the same morphology everywhere and does not tend to reproduce the more common myxomatous form of embryonal fat." Five of the 41 cases reported by Stout were of this round-cell type. No follow-up records were

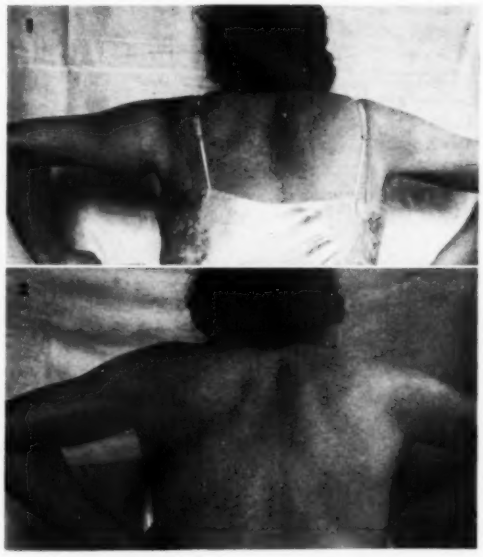

Fig. 1. Liposarcoma of soft tissues of the arm of a woman 29 years of age. There was a history of rapid growth following accidental discovery of the tumor six months previously.

Fig. 2. Appearance three months after surgical excision and interstitial radium treatment, and two months following completion of postoperative x-ray therapy.

available for 2 of his patients; 2 died in six and fifteen months, respectively, from pulmonary metastases; 1 is reported alive without recurrence after nine years. It would be difficult, if not impossible, to determine the number of cases of this type among the 134 other cases recorded in the literature, but it is evidently small. The rarity of the type, coupled with the fact that this patient was treated by both surgical and radiotherapeutic procedures, kept under observation six years and three months after she was originally seen, and then studied at autopsy, would appear to warrant the following report.

CASE REPORT

A white woman, aged 29 years, married and the mother of three children, was referred on Feb. 13, 1938, for consultation respecting a swelling in her left arm and a painful mass in the pelvis. She had first noticed the swelling in the arm six months previously, when it was the size of a hen's egg. She had been advised to apply hot fomentations, but these failed to have any effect on the swelling, which increased rapidly in size. Five weeks previous to

consultation, a severe pain in her abdomen caused her to faint. For two weeks she had had a high temperature, and for ten days there had been a purulent discharge from the rectum.

The mass in the left arm, situated immediately below the axilla, measured 9 × 9 × 7 cm. It seemingly was attached to the triceps muscle, was only slightly movable, and quite firm in consistency (Fig. 1). It was not attached to either skin or bone. Pelvic examination revealed a large abscess, which was draining through the rectum. No other masses could be felt, and there was no lymphatic enlargement. The patient weighed 128 pounds; the loss from her usual weight of 175 pounds she attributed to dieting and to her recent pelvic trouble. X-ray examinations of the chest and left humerus were negative. The clinical impression was that the tumor was malignant, probably either a myosarcoma or a fibrosarcoma, and that the pelvic abscess was entirely coincidental.

Roentgen irradiation of the tumor was advised as a preliminary to surgical removal; 200 r, measured in air, was given for each of 8 daily doses at 200 kv., 20 ma., and 50 cm. S.T.D., through two 10 × 15-cm. portals, with a Thoraeus "A" filter. No apparent change in the tumor resulted during this time, but there was a marked improvement in the pelvic condition, with subsidence of the temperature to normal and a blood count indicative only of secondary anemia.

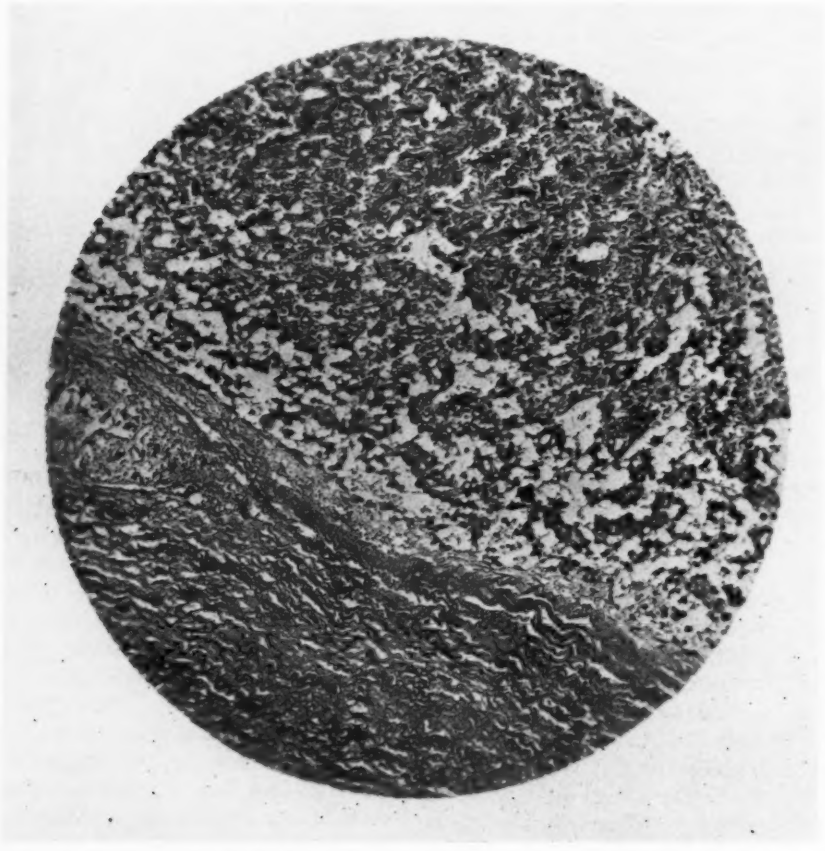

Fig. 3. Photomicrograph of primary tumor. A fibrous stroma separates masses of rounded cells into large groups. Many of these cells are vacuolated, foamy, and contain fat. *Diagnosis:* Liposarcoma of round-cell or adenoid type.

Operation was performed on Feb. 21, 1938. A vertical incision some 20 cm. in length was made over the posterior border of the deltoid. The deep fascia was opened, the deltoid was retracted forward, and the long head of the triceps posteriorly, exposing the brachial vessels and radial nerve. An encapsulated, soft, yellowish tumor was found lying beneath the deltoid and intimately attached to, and seemingly arising from, the lateral margin of the lateral head of the triceps. A small quantity

of gelatinous substance was escaping from a minute rupture of the capsule posteriorly. The capsule, bound down by delicate adhesions, was enucleated in an otherwise intact manner, and without difficulty, from all areas except the lateral head of the triceps, a portion of which muscle was removed along with the tumor. The excision appeared to surround the growth completely. Five 10-mg. and three 5-mg. radium element needles with 0.6 mm. of platinum filtration were implanted in the long

sists of polyhedral cells with nuclei of various sizes; many of these cells are vacuolated; in some areas the cells are more spindle-shaped. A considerable fibrous stroma divides the cells into large groups. At one point there is definite invasion of the capsule, with growth extending into the surrounding muscle tissue. Some areas are fairly vascular, and there is some haemorrhage into the tissue. A few mitotic cells are present. Fat stain shows the vacuolated cells to contain fat." (Fig. 3.)

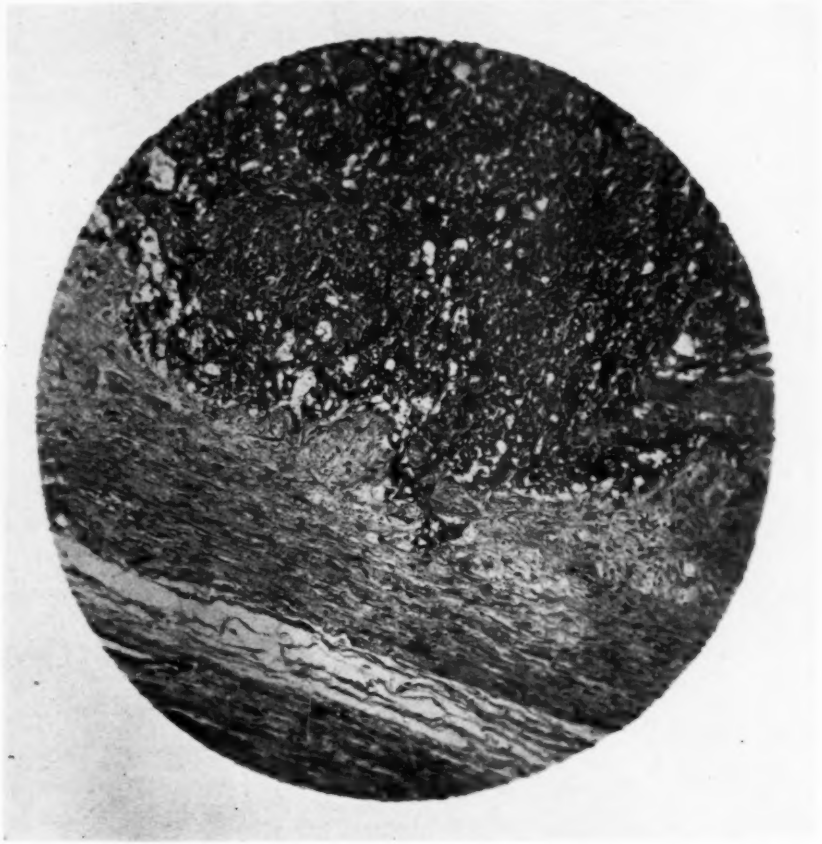

Fig. 4. Photomicrograph of recurrent nodule from beneath the operative scar, three and one-half years after removal of primary tumor. In comparison with the original tumor, the recurrence contains more fairly large, polyhedral cells, with fewer vacuoles, and more numerous mitotic figures.

head and severed margin of the lateral head of the triceps, and the posterior border of the deltoid, for a dose of 1,825 mg. hr.

The pathological report was as follows:

"*Macroscopic:* The specimen consists of an encapsulated new growth 10.5 × 7.5 × 4.5 cm. in size. The cut surface is soft and irregular, with an area showing considerable haemorrhage into the tissue.

"*Microscopic:* The majority of the growth con-

"*Pathological Diagnosis:* Liposarcoma."

The wound healed normally, and a course of postoperative roentgen irradiation through four portals was begun on March 1, utilizing the same factors as before, for a total further dosage of 4,400 r; this was completed on March 30. On April 22, the patient had a well developed erythema, but no actual blistering; there had been a gain of 16 pounds in weight. On May 20, the skin was normal (Fig. 2).

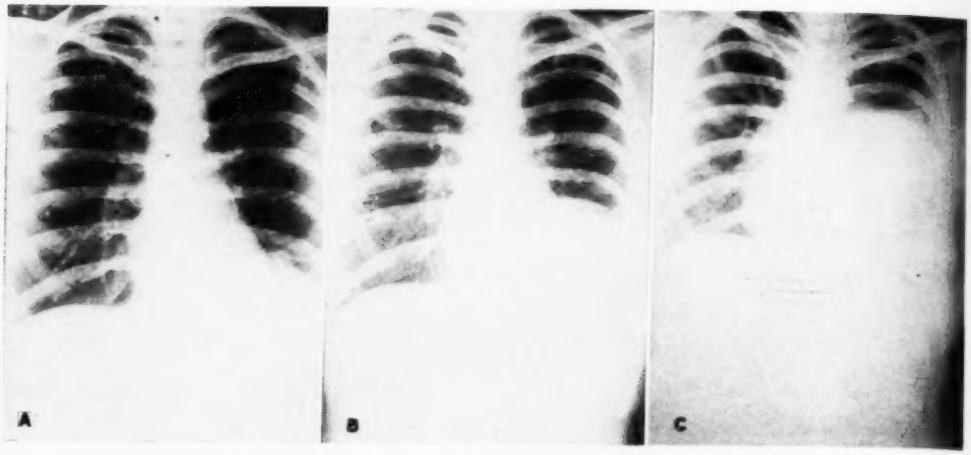

Fig. 5. Roentgenograms of chest showing the rapid growth of the metastatic tumor. A. Nov. 8, 1943. B. Jan. 15, 1944. C. March 9, 1944, six years after removal of the original lesion in the arm.

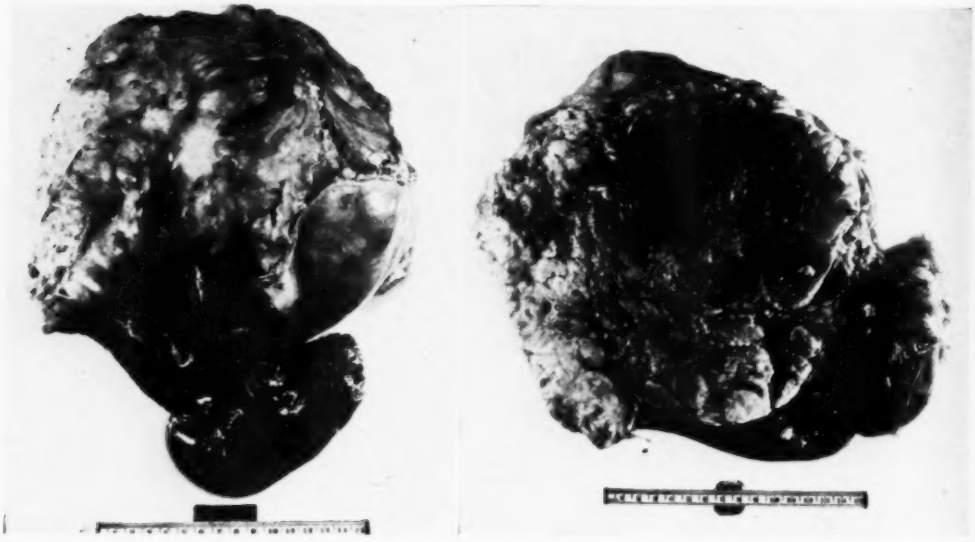

Fig. 6. Incompletely encapsulated pulmonary metastasis six years and three months after first admission.

Examination at regular intervals during the ensuing three years showed no evidence of the growth or change in weight, but on Aug. 22, 1941, a nodule 12 mm. in diameter was found immediately beneath the skin, 1 cm. medial to and 3 cm. above the lower end of the operative scar. This was excised on the following day, through an elliptical incision 6 cm. in length and 3 cm. in width, with removal of the underlying superficial fascia and outermost fibers of the triceps muscle. The nodule was encapsulated and appeared to be entirely removed. Four 5-mg. radium element needles were inserted in the triceps muscle beneath the site of excision, and the wound was closed with silk. The needles were left in place for 73 1/4 hours, giving a dose of 1,470 mg. hr.

The pathological report was as follows:

"*Macroscopic:* A diamond-shaped area of skin 4 cm. long and 2 cm. wide at the broadest portion, with an area of fatty and fibrous tissue 5.0 × 4.0 × 1.5 cm. in size. In the center of the latter is a small encapsulated area 1.5 cm. in diameter.

"*Microscopic:* The sections consist of a new growth of fairly large round cells, many of the foam-cell type. There is definite invasion of the muscle. In comparison with the original tumor, the recurrence contains more fairly large polyhedral cells

with fewer vacuoles and numerous mitotic figures (Fig. 4.). *Diagnosis:* Liposarcoma."

The wound healed slowly, a small necrotic area at its base persisting for several months, but without any evidence of further recurrence of the tumor; and the next summer the patient underwent an operation for the coexisting pelvic inflammatory disease.

The patient continued to report regularly for examination, and on Nov. 5, 1943, a second recurrence was observed, as a rounded, moderately firm mass, 5 × 4 cm., in the substance of the triceps muscle, high up beneath the upper portion of the scar. A chest film at this time (Fig. 5, A) showed a large area of consolidation above the left diaphragm, extending as high as the level of the 9th interspace posteriorly. An additional course of 200-kv. therapy was given to the axillary region, centered over the tumor in the arm, 4,200 r being delivered to this area between Nov. 8 and Dec. 1, 1943. By Dec. 16 the mass was very much smaller and barely palpable. Although the patient's weight had been maintained at 140 pounds, she began to suffer considerably from pleuritic pain, and on Jan. 15, 1944, the chest examination was repeated. The area previously noted was found to be more extensive and of greater density than on Nov. 8, now reaching to the level of the 8th interspace (Fig. 5, B). On March 9, 1944, 1,000 c.c. of clear yellowish fluid were withdrawn from the pleural cavity. A film now showed complete obliteration of the lower two-thirds of the left lung field with considerable fluid still present (Fig. 5, C). Two days later another 700 c.c. of fluid were withdrawn. Subsequent deterioration was rapid, and death occurred on May 25, 1944.

Fig. 7. Photomicrograph of pulmonary metastasis. The morphology of the primary tumor is maintained, with no tendency to reproduce the more common myxomatous form of embryonal fat.

At autopsy several pints of straw-colored fluid were found in the left pleural cavity. An incompletely encapsulated tumor, 28 × 22 × 15 cm. (Figs. 6 and 7) occupied the lower lobe of the left lung and was adherent to the posterior pleural wall, the diaphragm, and the surface of the pericardium.

The upper lobe was collapsed. The entire lung weighed 3,650 gm. There was no other demonstrable growth in the thoracic or abdominal cavities, and no gross evidence of tumor at the site of the last local recurrence under the operative scar on the arm; this area unfortunately, however, was not examined microscopically.

DISCUSSION

The encapsulation of these tumors is apt to delude one into proffering a good prognosis, whereas all authors agree that recurrence and ultimate metastasis are the rule, although in Geschickter's series (5) an average period of ten years elapsed between the first complaint and the occurrence of known metastases.

The location of the tumor in the case here reported was such that amputation was believed to offer little prospect of satisfactorily eliminating the disease, with the result that the patient was treated more or less in accordance with the recommendations of Ewing (4), who states that "the high mortality following surgical extirpation, together with the considerable radiosensitivity of many of the tumors, especially the myoliposarcomas, seems to call for a conservative program . . . involving diagnosis by aspiration, external radiation, followed by interstitial radiation if required, and surgical resection of the residual tumor if demanded." While failure of the primary tumor to respond visibly to 1,600 r of roentgen radiation, in the case reported, is indicative of at least moderate radioresistance, 4,200 r caused regression in size and ultimate macroscopic disappearance of the final local recurrence. The fact that these local recurrences did, however, take place, despite initial heavy postoperative irradiation, makes it appear unlikely that cure can be obtained by such means. Amputation has seldom been resorted to in these cases, probably because the location of the tumor so often renders it impossible or, at the most, highly undesirable, but the bad end-results so far obtained would cause the author to recommend an adequate course of preoperative roentgen irradiation followed by amputation wherever possible.

SUMMARY

Liposarcomas are rare but on occasions add to the interesting diagnostic and therapeutic problems of a tumor clinic.

The tumor in the case reported is one of the less common round-cell forms, simulating brown fat, rather than the more commonly encountered myxomatous type which resembles embryonal fat.

The patient remained free from any evidence of her disease for three and one-half years following excision and radiotherapy and then had a recurrence in the lower end of the operative scar. This was satisfactorily obliterated, and she remained clinically free for a further period of two years, when another recurrence developed nearby, as well as metastasis to the lung, which caused death six years and three months after the original admission.

To date, local recurrences and ultimate death from metastases have been the rule in cases of this disease.

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Albers-Schönberg Disease—A Family Survey[1]

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ALBERS-SCHÖNBERG disease or "marble bones" is a disease of unknown etiology, familial in occurrence, and characterized by an increase in the radiographic density of the bones, but with preservation of their structural contour. The condition is usually widespread throughout the skeletal system. On roentgenograms the bones appear almost homogeneous in consistency, and differentiation between compact and cancellous bone is absent. Progressive anemia, which is characteristically seen in the disease, is probably explained by the destruction of the bone marrow by the lime deposits. The base of the skull is frequently involved, and the foramina of exit for the cranial nerves are narrowed. This results in pressure on the cranial nerves, with such sequelae as facial palsy or paralysis, speech defects, deafness, optic atrophy, etc. The presence of some of these sequelae, namely, partial facial paralysis, bilateral impaired hearing, and a speech defect, along with intractable headache, was the clinical reason for the reference for roentgenograms of the skull of our first patient with Albers-Schönberg disease. After the disease was recognized in the first patient, roentgenograms of all members of the family were subsequently made, a procedure which should be followed wherever possible. This survey included all ten children of the family, the two parents, two sisters of the mother, and

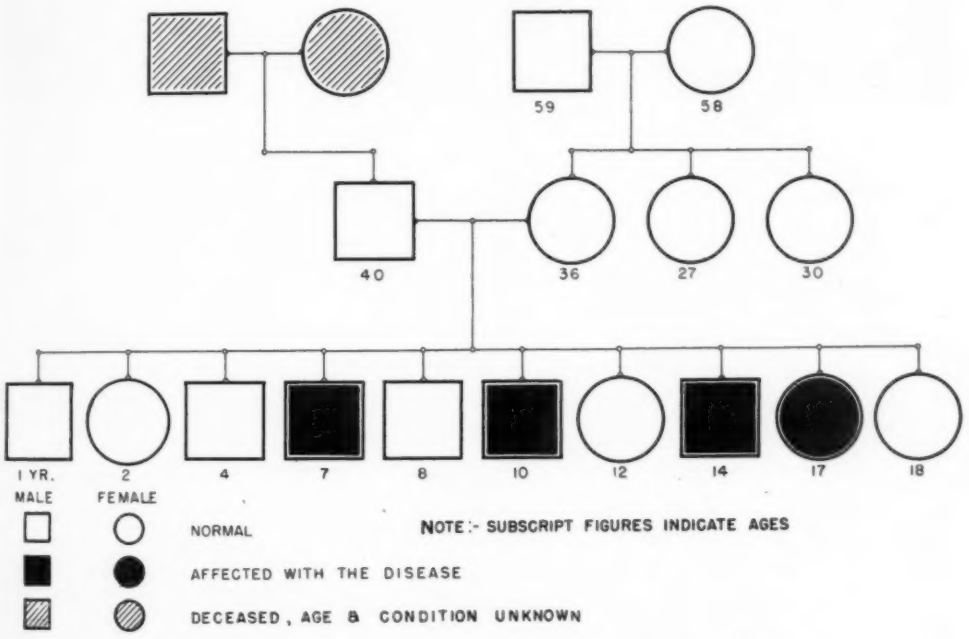

Chart I. Incidence of Albers-Schönberg disease in three generations.

[1] From the X-Ray Department of Freedmen's Hospital and Howard University College of Medicine, Washington, D. C. Accepted for publication in December 1945.

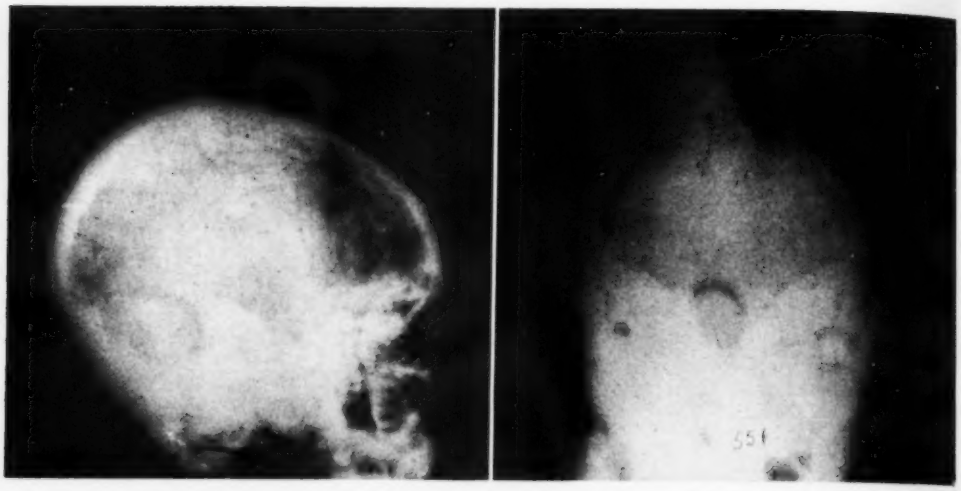

Fig. 1. Case I. Two views of the skull (left lateral and with occiput down). There is a homogeneous increase in density of all the bones, with thickening of skull tables. Diploic bone is as dense as the cortical layers.

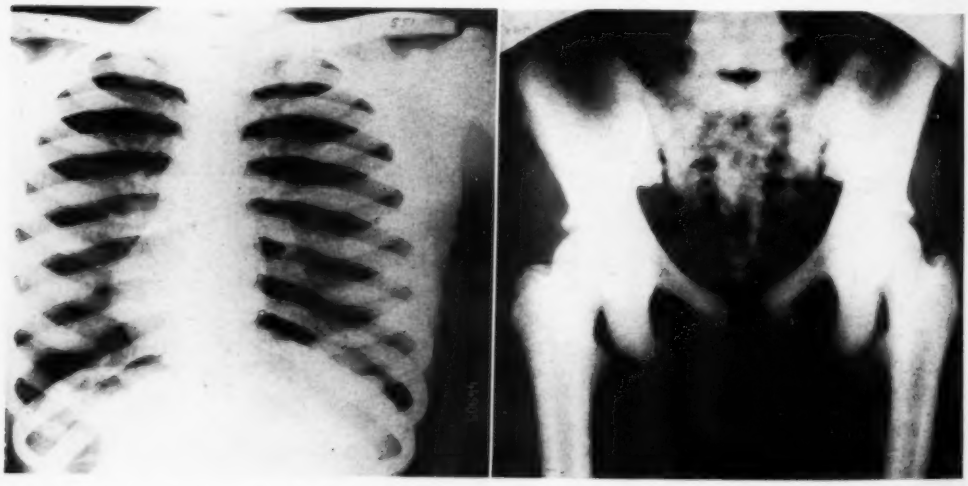

Fig. 2. Case I. Postero-anterior chest film and anteroposterior film of pelvis and upper femora. The bony thorax, pelvis, and upper ends of both femora show the dense, compact changes of the disease.

both maternal grandparents. The paternal grandparents were deceased. The disease was found in four of the children but in none of the other members of the family. Chart I summarizes the incidence of Albers-Schönberg disease in three generations of the family under discussion. Case histories of the affected members of the family follow:

CASE I (Figs. 1–4): E. G. P. was the first one of the family to be studied radiographically. She is a 17-year old Negro female, appearing much older. Her requisition for examination read: "Disorder of 7th and 8th cranial nerves and intractable headache." Her facial expression was blank and grotesque. She was unable to wrinkle her forehead or smile. Her mouth was small, with thin lips, and drawn to the left. Hearing was impaired on both sides. Her mentality was subnormal, with difficulty in remembering and inability to reason well. Her speech was slow, with a nasal quality, and difficult to understand.

The Hinton and Eagle tests were normal. The blood findings were: hemoglobin 60 per cent; red cells 4,380,000; white cells 8,250; acid phosphatase,

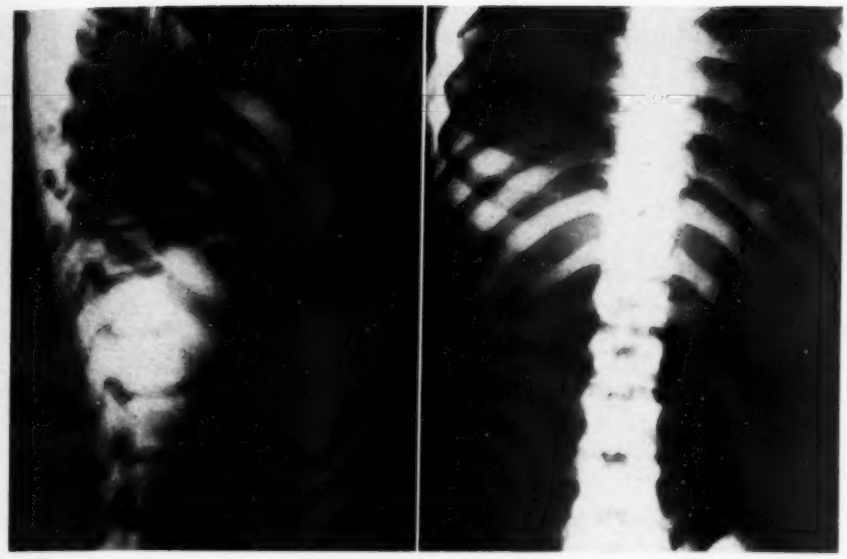

Fig. 3. Case I. Left lateral and anteroposterior views of the thoracolumbar spine. The bodies of the vertebrae are extremely dense and appear almost homogeneous in consistency.

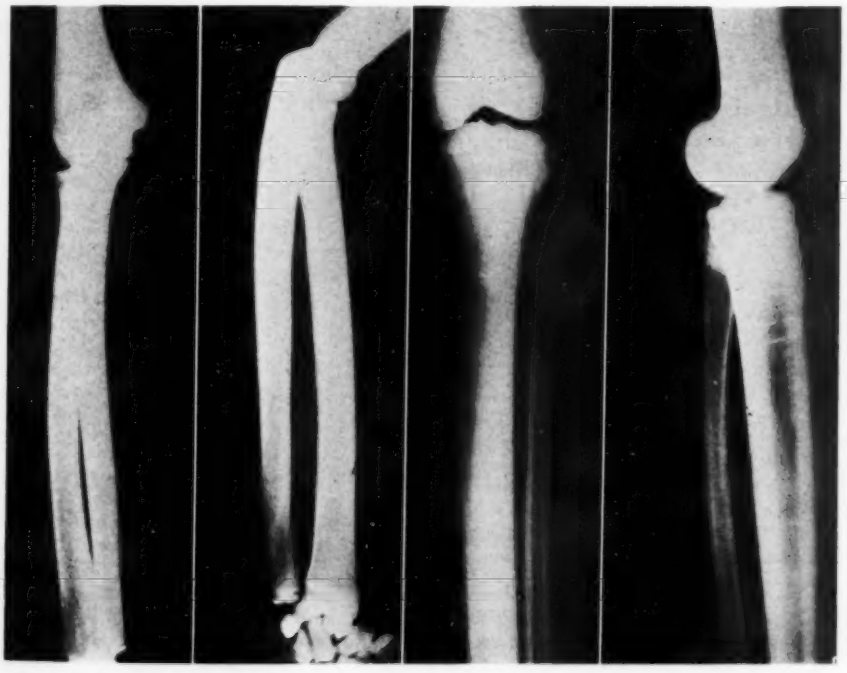

Fig. 4. Case I. Anteroposterior and lateral views of right forearm, and of the left tibia, fibula, and knee joint. There is a marked increase in density in these bones. Note that the patella also is increased in density.

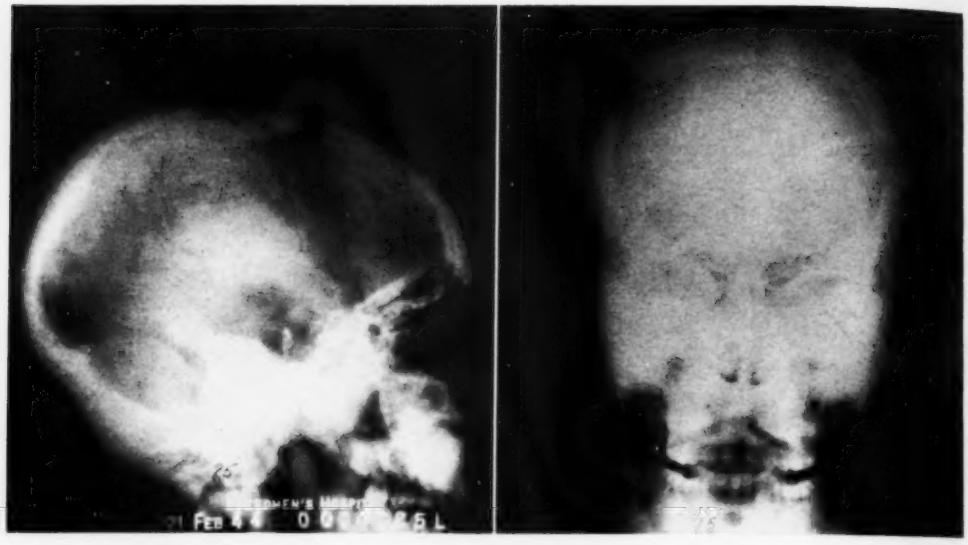

Fig. 5. Case II. Left lateral view of skull and view with occiput down. Thickening of the tables and marked homogeneous increase in density of all the skull bones are apparent.

0.4 unit; alkaline phosphatase, 3 units; calcium, 8.4 mg. per 100 c.c. Visual fields were diminished bilaterally.

Roentgenographically all the bones forming the skull were dense, with unusual thickening of the tables. In some places these measured 2.5 cm. Diploic bone appeared as dense and compact as cortical bone. The optic foramina were narrowed. The thoracic cage, pelvis, and bones of the upper and lower extremities showed similar dense, compact changes. Changes in the epiphyses were similar to those in the shafts.

CASE II (Figs. 5 and 6): M. P., a Negro male 14 years old, like his sister (Case I), appeared older than the age given. His mouth was drawn to the left. His hearing was impaired on both sides. His speech was not clear and, as in the case of his sister, his mentality was below normal. Severe headaches had been present over many months. Laboratory findings showed moderate secondary anemia with 70 per cent hemoglobin. Serologic studies, calcium, phosphorus, and phosphatase were within normal limits. The visual fields were diminished bilaterally.

Roentgenograms of the skull, thorax, pelvis, and long bones showed severe dense bone changes of Albers-Schönberg disease. Both optic foramina were narrowed.

CASE III (Fig. 7): T. L. P., a Negro male 10 years old, had right-sided weakness of the facial muscles, but the mouth was not drawn to the side. Hearing was slightly impaired on both sides. The patient appeared more intelligent than the two previously described (Cases I and II). Visual fields were diminished on both sides, but less so than in the two previous cases. Laboratory tests, carried out as in Cases I and II, showed no abnormal findings with the exception of a moderate secondary anemia.

Dense changes of Albers-Schönberg disease were demonstrable roentgenologically in the bones of the skull, thorax, pelvis, and extremities, but were less severe than in the preceding cases.

CASE IV (Fig. 8): V. T. P., a Negro male 7 years of age, had bilateral impairment of hearing and right-sided facial weakness, but paralysis of the facial nerve had not taken place. He appeared mentally retarded. The Hinton and Eagle tests were negative. Hemoglobin was 70 per cent, the red cell count 2,440,000, white cell count 7,050. Calcium, phosphorus, and phosphatase were within normal limits.

Roentgenograms showed bone changes in the skull, thorax, pelvis, and long bones characteristic of early Albers-Schönberg disease.

CASE V (Fig. 9): The case of V. R. P., a 2-year-old sister of the other patients, is reported because of the discovery in roentgenograms of the skull of a foreign body (screw) approximately 2 cm. in length, deeply embedded in the soft tissues of the floor of the left inferior meatus of the nose. The screw was removed surgically with the child under general anesthesia. No one in the family knew how the screw got into her nose. The service done on this patient was a measure of compensation for the many trips from their tobacco farm in Maryland to the hospital necessary to complete this work. Roentgenograms of the child's skeleton were normal.

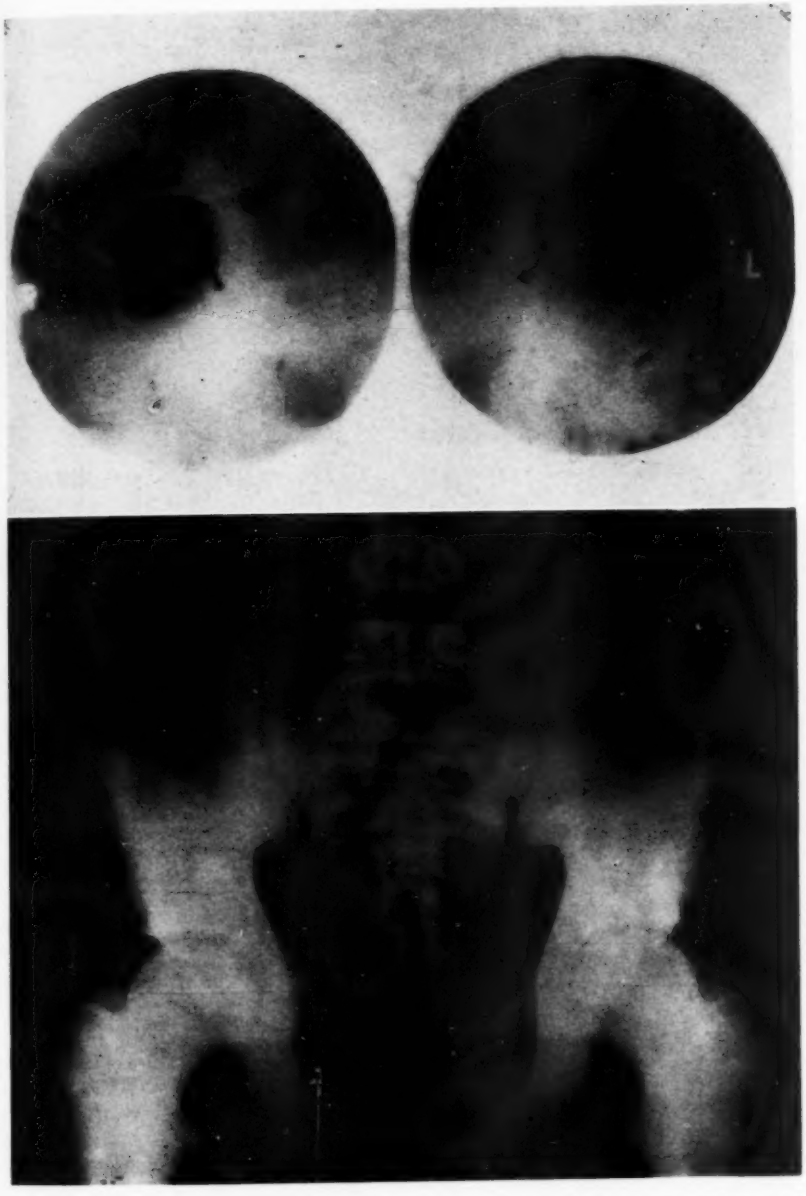

Fig. 6. Case II. Anteroposterior view of pelvis and right and left optic foramina. The pelvis and upper ends of both femora show marked homogeneous increase in density. Both optic foramina (indicated by arrows) are narrowed.

DISCUSSION

"Marble bones" was first described in the literature by Albers-Schönberg (1) in 1904, and the disease has become known as Albers-Schönberg disease. According to Pirie (4), up to 1929 a total of 26 cases had been published. Undoubtedly, a great number of additional cases have been seen by radiologists, some of which have been reported. The exact number, is not

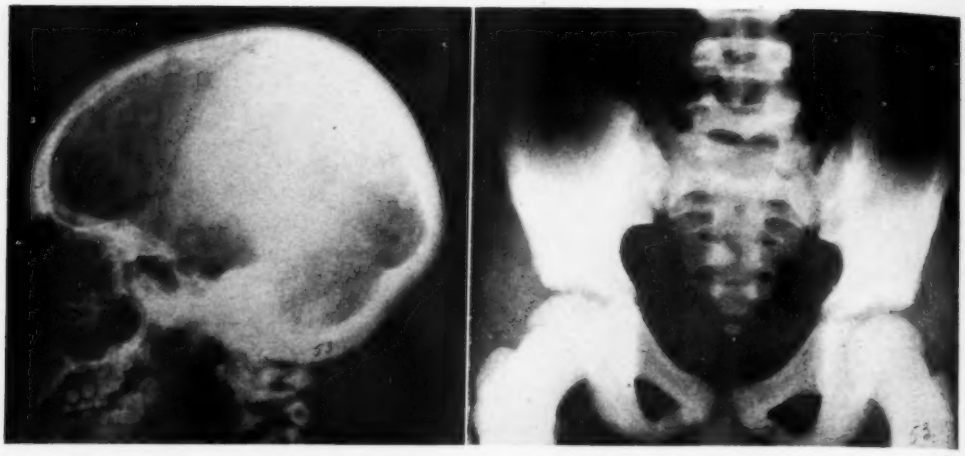

Fig. 7. Case III. Right lateral view of skull and anteroposterior view of pelvis. Both the skull and pelvis show fairly marked increase in density.

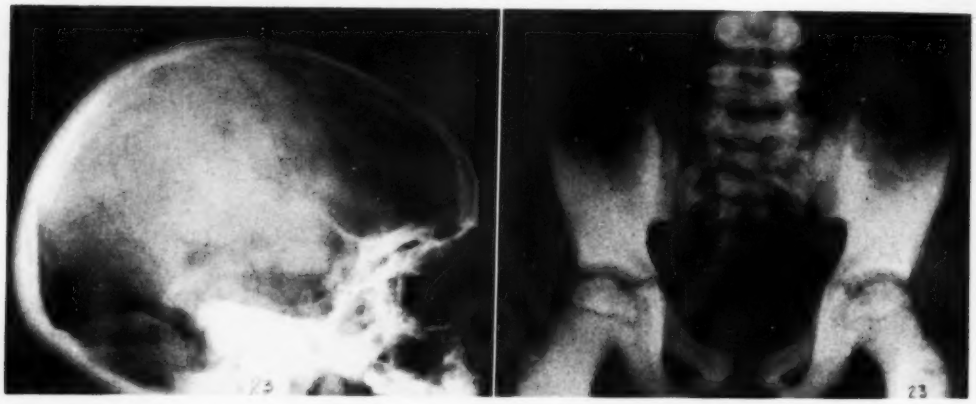

Fig. 8. Case IV. Left lateral view of skull and anteroposterior view of pelvis. Both the skull and pelvis show increase in density, but less marked than in Cases I, II, and III.

known. Excellent bibliographies are supplied by Pirie (4) and Alexander (2), and readers are referred to their papers.

While the etiology of the disease is unknown, its development has been studied by Pirie. He states that the condition begins to develop at the end of the diaphysis and extends into the shaft at or after puberty. Further, he suggests that, in view of the chalky consistency of the bones, which are easily cut by a penknife, and the frequency of fractures, the term "chalky bones" is more appropriate, the term "marble bones" being applicable only in consideration of the appearance on roentgenograms. There is, however, no general agreement among surgeons that the bones are of chalky consistency as is stated by Pirie.

According to Pancoast, Pendergrass, and Schaeffer (3), although the entire spine is frequently extensively involved, there is no stiffness of the vertebral joints and no encroachment on the intervertebral disks and spinal canal, and there is a remarkable freedom from any arthritic changes.

The severe disabilities attending the disease and its hereditary nature suggest that members of such families should not become parents.

CONCLUSIONS

1. Four cases of Albers-Schönberg disease occurring in the third generation of a family are reported.
2. A radiographic survey of all members of the second generation and the maternal half of the first generation of the family was made. No cases of Albers-Schönberg disease were found in this survey.
3. A short discussion of the nature of the disease is included.

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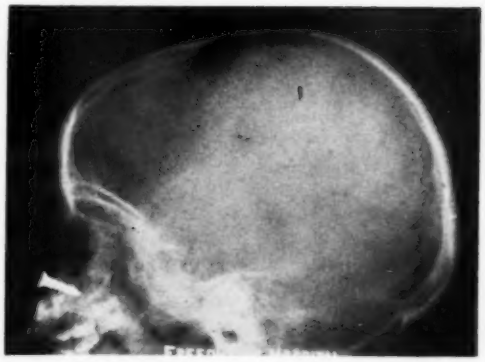

Fig. 9. Case V. Right lateral view of skull. Metallic screw present in upper nares, indicated by arrow.

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Eosinophilic Granuloma of Bone

Report of a Case with Preoperative Roentgen Diagnosis[1]

MAJ. PATRICK RILEY, M.C., A.U.S.

A 25-YEAR-OLD white soldier stationed in the South Pacific was in good health until the latter part of May 1944. At that time, upon lifting a heavy airplane engine part, he first experienced sharp, stabbing pain in the right axilla and beneath the right scapula. Motion of the right arm and shoulder, coughing, sneezing, and deep inspiration reproduced the pain. On occasions he was awakened at night by a heavy, dull aching sensation high in the right axilla.

Fig. 1. Roentgenogram of 2nd right rib. Note infiltrative destruction with minimal reaction, leaving islands of normal bone and eroding the cortex. Pathological fracture with callus is at the superior border.

Physiotherapy produced only moderate relief, and on June 3, 1944, the patient was admitted to a numbered station hospital. The only finding of significance on physical examination was sharp pain at the medial and inferior border of the right scapula when the arm was abducted beyond 90°. Roentgen examination of the right shoulder disclosed what was described as a localized osteolytic lesion of the 2nd right rib, containing remnants of normal bone. The remaining long bones, skull, and vertebrae showed no similar lesions.

[1] Accepted for publication in December 1945.

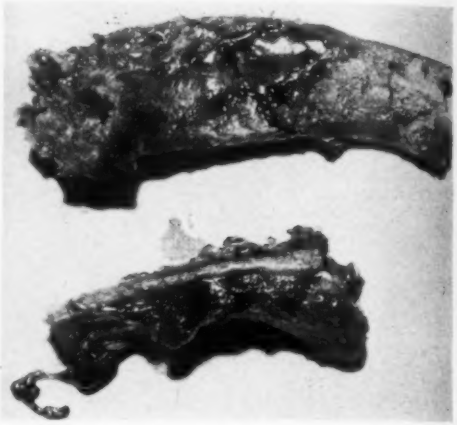

Fig. 2. Gross surgical specimen. Note pathological fracture completed at operation, and grumous mass perforating cortex.

Urinalysis gave normal findings, and tests for Bence-Jones protein were negative. Blood studies showed: hemoglobin 17.5 gm., white cells 10,650, with a normal differential count (3 per cent eosinophils), blood calcium 13.5 mg. and 13.0 mg. on two occasions, blood phosphorus 2.9 mg., sedimentation rate 8 mm. per hour (Cutler). A smear for malaria was negative, as was the Kahn reaction.

The patient was evacuated to the continental United States and admitted to a General Hospital on July 21, 1944. Physical examination was entirely negative at this time; range of motion of the right shoulder was normal, and there was neither pain nor tenderness in the axilla or shoulder girdle.

Laboratory findings were essentially the same as previously reported, except that the blood calcium was now 12.3 and 12.6 mg. on two occasions, the blood phosphorus was 3.9 and 4.7 mg., and phosphatase 9.2 units (Bodansky). Serum albumin was 4.88 gm. and serum globulin 2.42 gm.

The patient was referred to the roentgenological service for examination of the right shoulder, and the following opinion was given on July 27, 1944: "The 2nd right rib at the mid point of its shaft in the mid-axillary line presents an eccentric, oval-shaped area of infiltrative destruction with cortical erosion on the medullary side and moderate subperiosteal new bone formation. The lesion has grown in the axial plane of the rib, and though there is subperiosteal new bone formation, there is no soft-tissue mass surrounding the rib to give it a spherical shape. The area of destruction is fairly sharply demarcated,

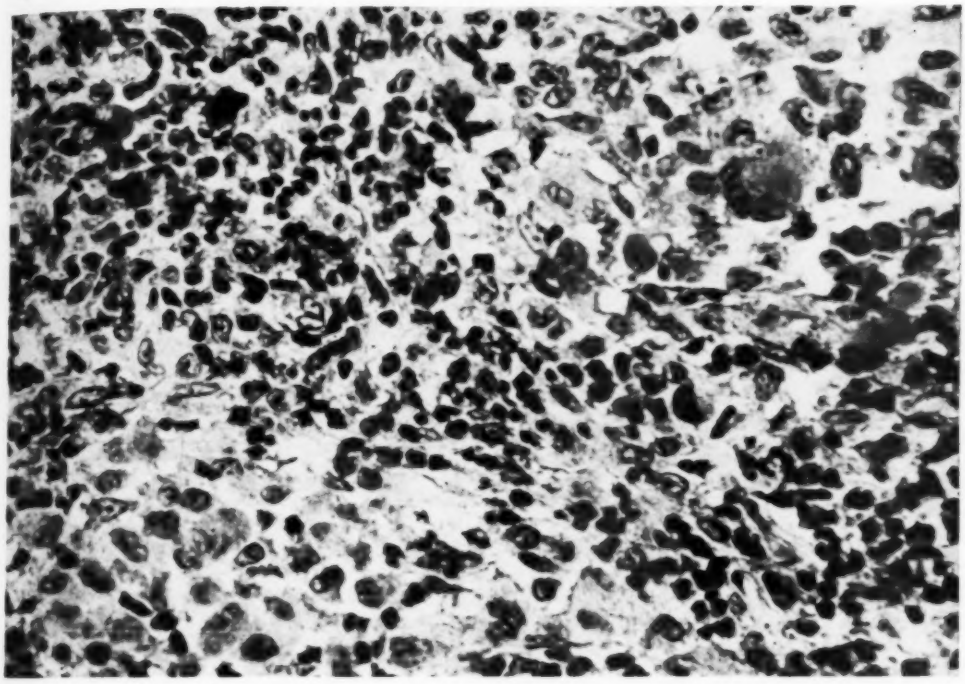

Fig. 3. Microscopic section of grumous mass. Note numerous small dark-staining eosinophils intermingling in sheets and cords between the large pale histiocytes. × *c.*450.

but at the margins the destructive process has infiltrated between the bony trabeculae, leaving small islands of normal bone between areas of destruction. Similarly, in the center of the lesion, where destruction has been most severe, a coarse reticulum of bone remains, giving a faintly honeycombed appearance. The lesion has not expanded the cortex, but it has eroded the cortex on the medullary side at the lower cortical margin. There is no heavy reactionary bone condensation surrounding the lesion, but a light narrow zone of reaction marks the limits of the more proximal margin of the area of destruction. There appear to be two small, incomplete pathologic fractures at the cortex. The area of destruction extends 5 cm. along the axial plane of the rib and 2 cm. across the transverse diameter.

"*Impression:* Although one is inclined to think of malignant neoplasm, criteria for malignancy are not readily evident, since the lesion is oval rather than spherical, because the destruction is infiltrative rather than invasive, and because the cortex is not broken through by the destructive process. On the other hand, the usual manifestations of inflammation are also absent in that there is little or no reactionary bone condensation or reactive subperiosteal calcification, and no soft-tissue mass. If the process is inflammatory, it must of necessity be of a very low grade of virulence. Expansile tumors, such as giant-cell tumor, are eliminated because of the absence of expansion of the cortex and of typical thin-walled trabeculation. Isolated myeloma of the plasma-cell type does not characteristically present the coarse reticulum or the subperiosteal new bone formation seen here. Osteitis fibrosa cystica would scarcely be expected to present the degree of subperiosteal new bone formation seen here. One destructive benign bone tumor which has been described as having all the characteristics of the lesion observed is solitary eosinophilic granuloma, and it is believed, therefore, that this is such a granuloma" (Fig. 1).

The involved portion of the 2nd right rib was then resected subperiosteally. At operation a pathologic fracture was found in the superior cortical border and, in removing the rib, an additional fracture occurred at the inferior border (Fig. 2). In the region where the destructive lesion was demonstrable on the roentgenogram there was a grayish-brown tumor of the consistency of guava jelly. This grumous mass completely occupied the destroyed area in the bone and had eroded the cortex severely. Both anteriorly and posteriorly the mass had pierced the cortex in several places and it was infiltrating the rib axially. The cortical perforation had not been apparent on the roentgenogram because superoinferior projection was not possible. The sub-

periosteal new bone described in the roentgen report is probably not an essential feature of the lesion, but rather callus resulting from the pathological fracture, as has been pointed out by Jaffe (1).

Histologic examination of the tissue (Fig. 3) disclosed extensive bone destruction. The essential cells were histiocytes of a large polyhedral variety possessing an abundance of pale, somewhat foamy cytoplasm intermingled with masses of eosinophils. In some sections the eosinophils were so numerous that they cast a red glow over the entire slide. The pathologic diagnosis was eosinophilic granuloma of bone.

The patient made an uneventful recovery and six months later was in excellent health and had experienced no further pain or disability in the right shoulder nor in any other organ or system. Roentgen examination revealed moderate progress toward inostosis of the rib defect. The blood calcium had fallen to 10.6 mg. and phosphatase to 2.5 units, while the blood phosphorus was 2.42 mg.

DISCUSSION

About 50 cases of eosinophilic granuloma of bone have been reported in the American literature. In only three publications (2–4) has it been mentioned that this entity was considered in the preoperative diagnosis, though undoubtedly it was taken into consideration by some of the authors who have reported several cases. The diagnosis was most often made after biopsy.

The present case is reported because the preoperative roentgen diagnosis was made with fair confidence, and for the purpose of drawing further attention to the entity so that it may more often be considered in differential diagnosis, thus avoiding unnecessarily extensive surgery, as when the lesion is mistaken for malignant neoplasm, or unnecessary drainage when it is mistaken for osteomyelitis.

Given a well localized lesion of bone, exhibiting characteristic infiltrative destruction with little or no surrounding reactive condensation, no soft-tissue mass, and no signs or symptoms other than local pain, in a relatively young person, eosinophilic granuloma of bone ought to be given serious consideration. The presence of multiple lesions should not of itself militate against the diagnosis, since that is not an uncommon occurrence.

124 So. Lasky Drive
Beverly Hills, Calif.

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"Iliac Horns" (Symmetrical Bilateral Central Posterior Iliac Processes)

A Case Report[1]

CAPT. E. E. FONG, M.C., A.U.S.

A CASE OF "ILIAC HORNS" (symmetrical bilateral central posterior iliac processes) is reported here because of the extremely unusual nature of the condition.

The patient presenting this anomaly was a 27-year-old woman with a mild hypertension developing during her first pregnancy. She failed to respond to pre-eclampsia treatment, and labor was induced on Sept. 17, 1944 A low forceps delivery was made after full dilatation of the cervix and an episiotomy. On Oct. 31, 1944, the vascular tension remained slightly elevated, but the urine had become free of albumin. The patient first came under the observation of the writer in January 1945, at which time intravenous pyelography was performed. Nothing unusual was demonstrated in the upper urinary tract, but bilateral smooth-surfaced bony protrusions were observed on the central portions of the ilia, and the patient was asked to return for further examination. On this subsequent examination (Figs. 1 and 2), the bilateral symmetrical iliac processes were found to arise from the posterior surfaces of the ilia. The processes measured approximately 2.5 cm. in diameter and projected laterally as well as posteriorly a distance of about 3 cm. The pelvic inlet was somewhat anthropoid in shape posteriorly. The inferior halves of the sacro-iliac joints were considerably more oblique than usual, so that a projection of lines drawn tangential to their surfaces would intersect at approximately a 90-degree angle at the sacrococcygeal junction. The plane of the lumbosacral articulation was more horizontal than usual. Although the patient had never realized the presence of the "iliac horns," these were easily palpable.

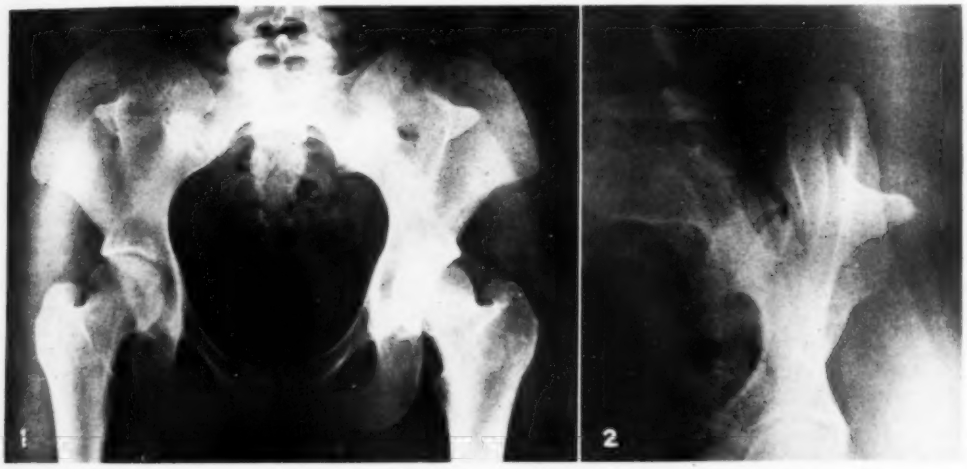


Fig. 1. Anteroposterior film showing the "iliac horns," the unusual obliquity of the inferior halves of the sacro-iliac joints, the rather horizontal lumbosacral joints, and the anthropoid type of pelvic inlet.
Fig. 2. Right posterior oblique film of the right ilium showing the base and posterior origin of one of the "iliac horns."

We were unable to recall ever having observed such "iliac horns" or reading any account of them. Since a search of the

[1] Accepted for publication in August 1945.

medical literature available to us failed to add any information, a copy of one of the films was sent to Dr. L. H. Garland for his opinion and assistance. He, too, had never seen such an anomaly and suggested a search of texts on comparative anatomy and enlistment of the help of the Director of the Army Medical Museum. The latter in turn referred the matter to Colonel A. A. de Lorimer, Commandant of the Army School of Roentgenology. A portion of his reply is quoted:

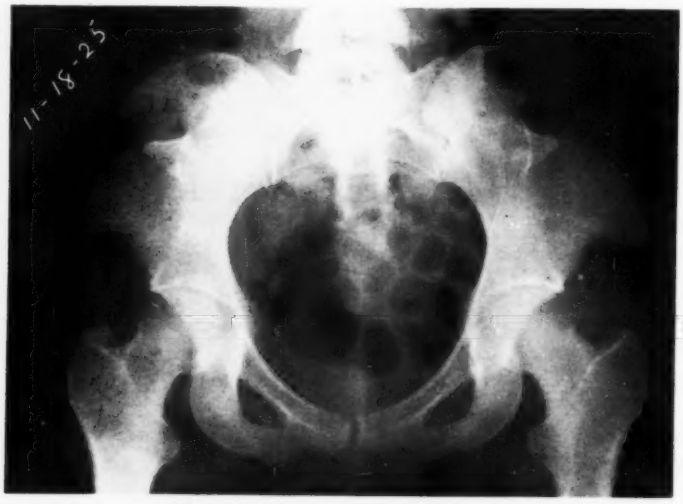
"An effort was made to find reference in the literature to this type of anomaly, but to no avail.

"We presented these films at one of our Monday evening sessions, where there were in attendance some thirty or forty doctors, including a dozen or more well qualified orthopedic surgeons (Drs. Speed, Boyd, Major Flanagan, Captain Haddon, and others from Kennedy General Hospital). No one has seen anything like your case."

Dr. Roland H. Alden of the Division of Anatomy, University of Tennessee College of Medicine, confirmed the results of our personal search and the opinion of Dr. J. R. Burkholder of the Fresno State College, (California) that there is no vertebrate animal which is normally equipped with these posterior "iliac horns."

We are unable to attach any useful function to the "iliac horns," or to explain their etiology.

331 Vernon St.
Oakland 10, Calif.



Editor's case observed in 1925. Note the similarity of the "iliac horns" to those in the author's patient.

EDITORIAL ADDENDUM

An anomaly similar to that described by the author was observed by the editor in 1925 as an incidental finding in the course of a routine urinary tract examination in a woman of 25 years. His report at that time reads: "There are spur-like processes coming off the posterior surface of both ilia just lateral to the sacroiliac joints. This is apparently a congenital anomaly." There was in this case an associated spina bifida occulta of the upper segment of the sacrum. A roentgenogram is reproduced for comparison with the case reported by Captain Fong, at whose request this note is added.

EDITORIAL

The Regional Irradiation in Malignant Neoplasms

In outlining the most efficient procedure of irradiation for malignant neoplasms, the knowledge of the various ways of metastasis is important. Surgical approach, as a rule, remains confined to the site of the original tumor and the primary regional area, but radiation therapy is much wider in scope. The formerly held view that if a tumor once has spread beyond the first barrier of regional defense the chances for success are practically eliminated does not conform to realities. The not insignificant percentage of five-year survivals in carcinomas with metastases to the secondary regional areas, or even more distant parts of the body, attests to this fact. A few examples are the 15 to 20 per cent five-year survival rate in carcinoma of the breast with metastases to the supraclavicular lymph nodes, a similar percentage in carcinoma of the cervix with invasion of the distant parametria, a 30 per cent five-year survival in lymphosarcomas and seminomas, these latter at times showing quite general metastases.

The major role in the dispersion of malignant neoplasms is played by the lymphatic system. Taylor and Nathanson (1) in an excellent treatise assembled all available information on the rather complicated anatomy of this system and the various factors affecting the distribution of cancer through the lymphatic pathways of different parts of the body. Their chief interest was to establish a proper background for the surgical management of the regional metastases.

According to the evidence found, the cells of malignant neoplasms continue to grow locally for a variable length of time; then they spread by means of emboli or diffuse permeation to the first region of lymph nodes. Here the metastases remain localized until progressive growth of the cells gradually leads to complete blockage of the lymph flow, when viable malignant cells are forced through fine vessels of anastomosis into the second region of lymph nodes. The process repeats itself, and a similar spread occurs to a third or fourth region of lymph nodes. Eventually the emboli of malignant cells reach the larger lymphatic ducts, being carried into the general blood circulation. According to Taylor and Nathanson, the significant fact is that in this centripetal spread the lymphatic vessels of the lower extremities, abdomen, and part of the thorax merge into the thoracic duct, which ascends through the posterior mediastinum and, after being joined by the trunks of the left upper extremity and of the left side of the neck, empties at the junction of the left internal jugular vein into the left subclavian vein. On the right side, only the considerably smaller trunks of the right upper thorax, right upper extremity, and right side of the neck empty, united or independently, into the corresponding jugulo-subclavian junction.

The most common regions of lymphatic dissemination in malignant neoplasms of a given location are well known and need not be mentioned here. A classical example is the carcinoma of the breast, where the first region lies in the axilla, the second in the supraclavicular fossa, the third in the supraclavicular fossa of the opposite side, and so on. There are, however, certain regions in which the mode of spread is not so evident and therefore their discussion may not appear out of place. Of these, the retroperitoneal and supraclavicular regions occupy the most prominent place.

Attention was first called to the significance of the retroperitoneal region by Desjardins (2) in 1939, who found that it is a metastatic station for a surprisingly large number of malignant tumors. The lymph nodes located in this area form a continuous system with the pelvic lymph nodes. For practical purposes the entire system may be divided into external iliac, internal iliac, common iliac, para-aortic, and mesenteric. The external iliac and internal iliac lymph nodes are located along the corresponding blood vessels and extend up to the bifurcation of the common iliac vessels, whence they continue as the common iliac lymph nodes up to the bifurcation of the abdominal aorta and the inferior vena cava. At this point the two common iliac chains unite to form the para-aortic lymph nodes, which follow the abdominal course of the aorta up to the diaphragm. The mesenteric lymph nodes are arranged along the superior mesenteric artery and its branches.

The regional spheres and the rather complicated interanastomoses of all these lymph node groups conform to the usual pattern, with the exception of the para-aortic group. As a rule, the lymph nodes receive lymph from the organs or tissues of the immediate neighborhood and thus their involvement constitutes the primary or secondary regional dispersion of a near-by malignant tumor. With the para-aortic lymph nodes it is different.

Desjardins described the para-aortic lymph nodes as a chain of twenty-five to thirty rather large nodes lying in front, behind, and to each side of the abdominal aorta and the inferior vena cava. Lymph from organs and structures of the corresponding side of the abdomen flows into them, but there is also anastomosis between the nodes on the right side and those in front or behind the vessels. The upper nodes of the group, moreover, receive a series of lymphatic channels on each side directly from the testis and ovary. These channels follow the course of the spermatic artery in the male and of the ovarian artery in the female. It is interesting that, whereas in other locations of the body the lymphatic vessels are closely related to the venous system, in the abdomen they are closer to the arteries. The mesenteric lymph nodes also communicate with the para-aortic lymph nodes.

The implications to the radiologist from a more careful study of the retroperitoneal region are manifold. In the first place, it becomes evident that radiation therapy to be successful must be extended beyond the site of the original tumor to include the primary regional and, whenever possible, the secondary regional lymph node metastases. This applies to practically all malignant neoplasms situated within the pelvis or abdomen. Secondly, in case of tumors of the ovary and testis, the upper para-aortic lymph nodes constitute the primary regional area. Only after the tumors have broken through the capsule of these organs and invaded the surrounding structures does the path of lymphatic dispersion change. In ovarian tumors, owing to the situation of the organ, the extension of the malignant process is mostly by implantation of the peritoneum, with subsequent metastases to other lymph node areas and to most of the abdominal viscera. In tumors of the testicle, the rupture of the capsule is followed by invasion along the vas and metastasis to the groin. It appears necessary, therefore, to include the upper para-aortic lymph nodes in the irradiation of all cases of malignant neoplasms of the ovary and testis. This means that the entire pelvis and abdomen must be treated. In the case of seminomas of the testicle, the irradiation is even extended to the chest and both supraclavicular regions. Thirdly, it was noted that in lesions of the lymphatic system proper, the retroperitoneal and in particular the para-aortic lymph nodes often form obscure metastatic stations for a primary focus of almost any location. In other, not altogether rare instances, they constitute the seat of the primary manifestation of the disease, which may remain hidden for a considerable length of time before a more tangible dispersion occurs.

In connection with this latter, Desjardins (3) observed, for example, that the appearance of fever, itching, and cutaneous disturbances during the course of lymphosarcoma or Hodgkin's disease is always indicative of involvement of retroperitoneal lymph nodes, even though no tumor may be palpable. The rapid clearing up of the symptoms following irradiation of the upper abdomen furnishes additional proof of the correctness of the diagnosis. In like manner, a favorable response to irradiation of the upper abdomen points to a primary lymphosarcoma or Hodgkin's disease of the para-aortic lymph nodes when no other diagnostic signs are available. Craver and Herrmann (4) in a recent publication analyzed 406 cases of Hodgkin's disease treated at Memorial Hospital (New York) from 1932 to 1942, inclusive, and found that in 11 per cent there were symptoms suggesting extrinsic gastro-intestinal involvement, most frequently in the retroperitoneal lymph nodes. An even higher incidence has been noted by other investigators.

The significance of the supraclavicular region in the dispersion of malignant neoplasms was studied in detail by Viacava and Pack (5). From a purely clinical point of view the lymph nodes in this region may be divided into two groups: those receiving the afferents from the head, neck, upper portion of the pectoral region, and part of the arms, and those communicating by means of efferents with the brachial groups of the axillary lymph nodes and with the thoracic duct on the left side and the large lymphatic duct or its three branches on the right side. In the first group, primary regional metastasis may occur from malignant neoplasms of the oral cavity, sinuses, pharynx, larynx, and the structures of the skin. In the second, the invasion represents a secondary or tertiary regional spread in a successive chain of lymphatic dissemination by emboli. At times the invasion may occur without affecting the intermediate parts of the chain, in which instance the supraclavicular metastases may constitute the primary regional dispersion from a more distant focus, as, for example, a carcinoma of the ovary or rectum. The situation is similar to the primary regional metastases in the groin from a malignant neoplasm of the toe, when no other intermediate parts of the lymphatic system of the lower extremity are involved.

Viacava and Pack made a statistical compilation of 4,365 patients with abdominal and thoracic tumors who were treated in the last two decades at Memorial Hospital and found that 122 of these, or 2.8 per cent, presented histologically proved metastases to the supraclavicular region. In 73 patients the metastases were on the left side, in 31 on the right side, and in 18 there was bilateral involvement. Some interesting figures were obtained in regard to the incidence of the supraclavicular metastases from the various organs. For the lung, the figure was 2.8 per cent, for the esophagus 13.2 per cent, for the stomach 8.1 per cent, for the pancreas 8.1 per cent, for the kidneys 6.9 per cent, for the ovaries 6.1 per cent, for the corpus uteri 1.5 per cent, for the cervix uteri 0.8 per cent, for the testes 4.8 per cent, for the prostate 1.9 per cent, and for the rectum 0.2 per cent. No metastases to the supraclavicular lymph nodes were discovered in the records of patients with tumors of the small intestine, gallbladder, or urinary bladder. The metastatic involvement of the right supraclavicular lymph nodes and the bilateral invasion were observed chiefly in thoracic tumors, so that many of them undoubtedly represented primary regional dispersions. In 41 patients of the entire group the supraclavicular metastases constituted the first clinical sign of a malignant tumor, leading to a search for the primary focus.

As in the case of the retroperitoneal region, the early inclusion of the supraclavicular region in the general scheme of irradiation of all suspected cases helps to improve the final results.

The above considerations are important, also, from another point of view. Radical surgical dissection of the lymph nodes

should be contemplated only when there is ample evidence that the dispersion of the malignant cells is localized to the first regional area. After the dissemination has progressed to the secondary or tertiary lymph nodes, the malignant process is completely out of surgical control. Likewise, operative intervention will prove futile whenever the primary regional metastasis occurs above the customarily established level in the lymphatic chain.

T. LEUCUTIA, M.D.

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ANNUAL MEETING
LADIES' ENTERTAINMENT

Under the direction of Mrs. Harold E. Davis, the following program of Ladies' Entertainment has been arranged for the Chicago meeting. Fuller information may be obtained from members of the Chicago Women's Committee at the registration desk.

Sunday and Monday, Dec. 1 and 2

Registration at Palmer House.

Tuesday, Dec. 3, 11:00 A.M.

Tour of Chicago followed by

Luncheon in Club Room of Chicago Art Institute and

Conducted tour through Gallery of Masterpieces of English Paintings by Hogarth, Constable, and Turner, loaned by His Majesty the King, the Museums, and Collectors of Great Britain. (Tickets $3.00).

Wednesday, Dec. 4, 2:30 P.M.

Musicale and tea at the home of Mrs. Harold E. Davis, 419 Wellington Ave.

ALABAMA RADIOLOGICAL SOCIETY

A recent addition to the roster of state radiological societies is the Alabama Radiological Society, organized in April 1946. The officers are: Dr. J. A. Meadows, Birmingham, President; Dr. Courtney S. Stickley, Montgomery, Vice-President; Dr. John Day Peake, Mobile, Secretary-Treasurer. The next meeting of the Society will be held at the time and place of the meeting of the Alabama State Medical Association.

CHICAGO ROENTGEN SOCIETY

The newly elected officers of the Chicago Roentgen Society are: Earl E. Barth, M.D., President; Fay H. Squire, M.D., Vice-President; T. J. Wachowski, M.D., Secretary-Treasurer.

DR. JOHN S. BOUSLOG HONORED

At the annual meeting of the Colorado State Medical Society, Dr. John S. Bouslog was chosen President-Elect. Dr. Bouslog has long been active in the Society, and his election to this high office is a fitting recognition of his services. This is the second time within a two-year period that this honor has been bestowed upon a radiologist. Dr. George A. Unfug, elected in 1944, completes his term as President this year.

DR. ALBAN KÖHLER

Friends of Dr. Alban Köhler, of Wiesbaden, Germany, will be interested to have word of him after the long silence of the war years. In a letter addressed to Dr. James T. Case, Dr. Köhler writes in part:

"At last once more one can communicate with his good friends and colleagues. . . .

"I have suffered severely from reverses. In 1942 my dear wife was taken from me by death. The first of March 1945, my only son fell on the Eastern Front. He was a pediatrician in Mainz and left a wife and two small children. We, all four, live in a small health resort in which I practice, because, in February 1945, Wiesbaden was bombarded in a severe air attack and I had the misfortune that my house, my dwelling with the large roentgen institute in which I had done my important work, was completely burned down. I lost everything, including my historical library, one of the outstanding in the world, and I have up until now been unable to buy new apparatus.

"That we hunger, you know, but we must be very thankful to America that we are not starving. I have lost fifty-six pounds since the beginning of the war. It is obvious that I would be very fortunate if I could receive a little package, perhaps some honey and tea and a little chocolate."

Dr. Köhler's present address is 16 Nieder-Selters (Taunus), Bernwies 2, Gross-Hessen, Deutschland, American Zone.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

THE CHEST. A HANDBOOK OF ROENTGEN DIAGNOSIS. By LEO G. RIGLER, M.D., Professor and Chief, Department of Radiology, University of Minnesota. A volume of 352 pages, with 338 illustrations. Published by The Year Book Publishers, Chicago, 1946. Price $6.50.

MEGACOLON IN THE NEWBORN. A CLINICAL AND ROENTGENOLOGICAL STUDY WITH SPECIAL REGARD TO THE PATHOGENESIS. BY THEODOR EHRENPREIS. Supplementum 112 to Acta chirurgica Scandinavica, Vol. XCIV (94). A volume of 114 pages, with numerous illustrations. Published by P. A. Morstedt & Söner, Stockholm, 1946.

MONGOLISM AND CRETINISM. A STUDY OF THE CLINICAL MANIFESTATIONS AND THE GENERAL PATHOLOGY OF PITUITARY AND THYROID DEFICIENCY. By CLEMENS E. BENDA, M.D., Director, Wallace Research Laboratory for the Study of Mental Deficiency, Wrentham, Mass.; Instructor

in Neuropathology, Harvard Medical School, Assistant in Psychiatry, Massachusetts General Hospital; Lecturer, Postgraduate Seminar, Massachusetts Department of Mental Health. A volume of 310 pages, with 101 illustrations. Published by Grune & Stratton, New York, 1946. Price $6.50.

Book Reviews

LE FIBRO-MYOME UTERIN. By J. DUCUING, Professeur de clinique chirurgicale a la Faculté de Médicine de Toulouse. Directeur du Centre Anticancéreux. A paper-bound volume of 537 pages with 156 illustrations. Published by Masson & Cie., Paris, 1946. Price 735 francs.

This book of statistics, criticisms, and commentaries on a personal series of 1,300 cases of uterine fibroid (of which 547 have not previously been reported), together with a section on experimental production of fibromyomas and one on the physiology of the irradiated ovary, is a most unique presentation, quite different from the usual textbook. The subject of uterine fibroids—possibly a not important one—is presented in a way to hold the attention almost like a novel. The author, whose interest is primarily surgical, takes up, step by step, his conversion and reversal of opinion which have led him to favor roentgen rays rather than operation for the treatment of 80 per cent of fibroids. One is impressed by his honest, straight thinking and by the lucidity of his presentation. Ducuing has had a very large personal experience with the lesion in point, which entitles him to write with authority. In each sentence he seems to know exactly what he is writing about, and so does his reader.

Throughout the book one notices an over-emphasis on the works of French authors and, to a lesser extent, those of German authors, with a seeming neglect of American writers. This predominance of citation is explainable by the fact that the controversy between surgeons and radiologists over the treatment of fibroids has been more acute on the Continent than in the United States.

The volume is well illustrated and well printed (but not very well bound) on an excellent grade of paper. It has twelve chapters, an extensive bibliography, and a good index. It is not intended for students, but for those who already have some acquaintance with the subject, and may be recommended to every physician who is interested in uterine fibromyomas. It should appeal especially to surgeons, radiologists, and others who want to know the opinions of one thoroughly qualified to discuss the diagnosis and treatment of this condition.

PRÉCIS DE RADIODIAGNOSTIC. By P. VAN PÉE, Professor of Radiology at the University of Liége. A volume of 382 pages, with 214 figures and 62 roentgenographic prints. Published by Masson & Cie, Paris, 1946.

Van Pée's *Precis de radiodiagnostic* may be recommended as a compact handy reference book of diagnostic roentgenology. In a clear but concise manner it touches upon nearly every phase of the subject. It appears to have been written primarily for students, since the text is to a certain extent presented in short paragraphs, suggesting a syllabus for lecture purposes. Unfortunately, in the attempt to cover the whole field of diagnostic roentgenology in a compass of 382 pages, the author has had to present the subject matter in such a condensed form that some important information has necessarily been sacrificed.

The material presented is informative and represents a modern concept of diagnosis by a roentgenologist of wide experience. The author stresses the fact that while many conditions lend themselves to a definite roentgenologic diagnosis, most often the roentgenologist, being a physician, should have all the clinical and laboratory information concerning the case before reaching a final conclusion.

The text is well illustrated with diagrams and excellent photographic reproductions printed on heavy paper. A chapter on the physics of roentgen rays serves as a useful introduction to the chapters on diagnosis.

RADIOLOGICAL SOCIETIES OF NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate by sending information to Howard P. Doub, M.D., Editor, Henry Ford Hospital, Detroit 2, Mich.

UNITED STATES

Radiological Society of North America.—Secretary, D. S. Childs, M.D.,607 Medical Arts Bldg.,Syracuse 2, N.Y.

American Roentgen Ray Society.—Secretary, Harold Dabney Kerr, M.D., Iowa City, Iowa.

American College of Radiology.—Secretary, Mac F. Cahal, 20 N. Wacker Dr., Chicago 6, Ill.

Section on Radiology, A. M. A.—Secretary, U. V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio.

ALABAMA

Alabama Radiological Society.—Secy.-Treasurer, John Day Peake, M.D., Mobile Infirmary, Mobile.

ARKANSAS

Arkansas Radiological Society.—Secretary, Fred Hames, M.D., Pine Bluff. Meets every three months and annually at meeting of State Medical Society.

CALIFORNIA

California Medical Association, Section on Radiology.—Secretary, D. R. MacColl, M.D., 2007 Wilshire Blvd., Los Angeles 5.

Los Angeles County Medical Association, Radiological Section.—Secretary, Roy W. Johnson, M.D., 1407 South Hope St., Los Angeles. Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Secretary, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with California Medical Association.

San Diego Roentgen Society.—Secretary, R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego, Calif. Meets first Wednesday of each month.

San Francisco Radiological Society.—Secretary, Joseph Levitin, M.D., 516 Sutter St., San Francisco 2. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year in Lane Hall, Stanford University Hospital, and second six months in Toland Hall, University of California Hospital.

COLORADO

Denver Radiological Club.—Secretary, Washington C. Huyler, M.D., Mercy Hospital, Denver 6. Meets third Friday of each month, Colorado School of Medicine.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Secretary, Max Climan, M.D., 242 Trumbull St., Hartford 3. Meetings bimonthly, second Thursday.

FLORIDA

Florida Radiological Society.—Secy.-Treasurer, Maxey Dell, Jr., M.D., 333 West Main St., S., Gainesville.

GEORGIA

Georgia Radiological Society.—Secretary-Treasurer, James J. Clark, M.D., 478 Peachtree St., N. E., Atlanta 3. Meets in November and at the annual meeting of State Medical Association.

ILLINOIS

Chicago Roentgen Society.—Secretary, T. J. Wachowski, M.D., 310 Ellis Ave., Wheaton. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—Secretary-Treasurer, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Secretary, Frank S. Hussey, M.D., 250 East Superior St., Chicago 11.

INDIANA

The Indiana Roentgen Society.—Secretary-Treasurer, J. A. Campbell, M.D., Indiana University Hospitals, Indianapolis 7. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Secretary, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—Secy.-Treasurer, Sydney E. Johnson, M.D., 101 W. Chestnut St., Louisville.

LOUISIANA

Louisiana Radiological Society.—Secretary-Treasurer, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

Orleans Parish Radiological Society.—Secretary, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

Shreveport Radiological Club.—Secretary, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday, 7:30 P.M.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Secretary, Charles N. Davidson, M.D., 101 West Read St., Baltimore 1.

MICHIGAN

Detroit X-ray and Radium Society.—Secretary-Treasurer, E. R. Witwer, M.D., Harper Hospital, Detroit 1. Meetings first Thursday of each month from October to May, at Wayne County Medical Society club rooms.

MINNESOTA

Minnesota Radiological Society.—Secretary, A. T. Stenstrom, M.D., Minneapolis General Hospital, Minneapolis 26. Meetings quarterly.

MISSOURI

Radiological Society of Greater Kansas City.—Secretary, John W. Walker, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Friday of each month.

St. Louis Society of Radiologists.—Secretary, Edwin C. Ernst, M.D., 100 Beaumont Medical Bldg. Meets on fourth Wednesday of each month, October to May.

NEBRASKA

Nebraska Radiological Society.—Secretary-Treasurer, Donald H. Breit, M.D., University of Nebraska Hospital, Omaha 5. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND

New England Roentgen Ray Society.—Secretary-Treasurer, George Levene, M.D., Massachusetts Memorial

Hospitals, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW HAMPSHIRE

New Hampshire Roentgen Society.—Secretary-Treasurer, Richard C. Batt, M.D., St. Louis Hospital, Berlin.

NEW JERSEY

Radiological Society of New Jersey.—Secretary, W. H. Seward, M.D., Orange Memorial Hospital, Orange. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called.

NEW YORK

Associated Radiologists of New York, Inc.—Secretary, William J. Francis, M.D., East Rockaway, L. I.

Brooklyn Roentgen Ray Society.—Secretary-Treasurer, Abraham H. Levy, M.D., 1354 Carroll St., Bklyn. 13. Meets fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—Secretary-Treasurer, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Society.—Secretary-Treasurer, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse 10. Meetings in January, May, and October.

Long Island Radiological Society.—Secretary, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—Secretary, Wm. Snow, M.D., 941 Park Ave., New York 28.

Rochester Roentgen-Ray Society.—Secretary, Murray P. George, M.D., 260 Crittenden Blvd., Rochester 7. Meets at Strong Memorial Hospital, third Monday, September through May.

NORTH CAROLINA

Radiological Society of North Carolina.—Secretary-Treasurer, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

NORTH DAKOTA

North Dakota Radiological Society.—Secretary, Charles Heilman, M.D., 1338 Second St., N., Fargo.

OHIO

Ohio Radiological Society.—Secretary, Henry Snow, M.D., 1061 Reibold Bldg., Dayton 2. Next meeting at annual meeting of the Ohio State Medical Association.

Central Ohio Radiological Society.—Secretary, Hugh A. Baldwin, 347 E. State St., Columbus.

Cleveland Radiological Society.—Secretary-Treasurer, Carroll C. Dundon, M.D., 11311 Shaker Blvd., Cleveland 4. Meetings at 6:30 P.M. on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*Secretary-Treasurer,* Samuel Brown, M.D., 707 Race St., Cincinnati 2. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—Secretary-Treasurer, L. E. Wurster, M.D., 416 Pine St., Williamsport 8.

Philadelphia Roentgen Ray Society.—Secretary, Calvin L. Stewart, M.D., Jefferson Hospital, Philadelphia 7. Meets first Thursday of each month at 8:00 P.M., from October to May in Thomson Hall, 21 S. 22d St.

Pittsburgh Roentgen Society.—Secretary-Treasurer, Lester M. J. Freedman, M.D., 415 Highland Bldg., Pittsburgh 6. Meets second Wednesday of each month at 6:30 P.M., October to May, inclusive.

ROCKY MOUNTAIN STATES

Rocky Mountain Radiological Society.—Secretary, A. M. Popma, M.D., 220 N. First St., Boise, Idaho.

SOUTH CAROLINA

South Carolina X-ray Society.—Secretary-Treasurer, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston 16.

TENNESSEE

Memphis Roentgen Club.—Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—Secretary-Treasurer, J. Marsh Frére, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

TEXAS

Dallas-Fort Worth Roentgen Study Club.—Secretary, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meetings on third Monday of each month, in Dallas in the odd months and in Fort Worth in the even months.

Texas Radiological Society.—Secretary-Treasurer, R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth 4.

UTAH

Utah State Radiological Society.—Secretary-Treasurer, M. Lowry Allen, M.D., Judge Bldg., Salt Lake City 1. Meets third Wednesday, January, March, May, September, November.

VIRGINIA

Virginia Radiological Society.—Secretary, E. Latan Flanagan, M.D., 215 Medical Arts Bldg., Richmond 19.

WASHINGTON

Washington State Radiological Society.—Secretary-Treasurer, Thomas Carlile, M.D., 1115 Terry Ave., Seattle. Meetings fourth Monday of each month, October through May, at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary-Treasurer, C. A. H. Fortier, M.D., 231 W. Wisconsin Ave., Milwaukee 3. Meets monthly on second Monday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, S. R. Beatty, M.D., 185 Hazel St., Oshkosh. Two-day meeting in May and one day at annual meeting of State Medical Society in September.

University of Wisconsin Radiological Conference.—Meets first and third Thursdays 4 to 5 P.M., September to May, inclusive, Room 301, Service Memorial Institute, 426 N. Charter St., Madison 6.

CANADA

Canadian Association of Radiologists.—Honorary Secretary-Treasurer, E. M. Crawford, M.D., 2100 Marlowe Ave., Montreal 28, Quebec.

La Société Canadienne-Française d'Electrologie et de Radiologie Médicales.—General Secretary, Origéne Dufresne, M.D., Institut du Radium, Montreal. Meets on third Saturday of each month.

CUBA

Sociedad de Radiología y Fisioterapia de Cuba.—Offices in Hospital Mercedes, Havana. Meets monthly.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Digestive System

The Spleen

The Musculoskeletal System

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Intracranial Angiography. I. The Diagnosis of Vascular Lesions. Carl F. List and Fred J. Hodges. J. Neurosurg. **3:** 25–45, January 1946.

This article on intracranial angiography in the diagnosis of vascular lesions is of especial interest as a supplement to the paper by List, Burge, and Hodges in RADIOLOGY **45:** 1, 1945. The authors report their observations in 35 cases of vascular intracranial lesions, which they divide as follows: (1) vascular occlusions and coarctation, (2) intracranial aneurysms, (3) arteriovenous fistulas, and (4) congenital arteriovenous malformations. Eighteen illustrative case reports are included.

Arteriovenous Aneurysms of the Scalp and Face. Walter E. Dandy. Arch. Surg. **52:** 1–32, January 1946.

Nine cases of arteriovenous aneurysm of the scalp and face are reported, 8 congenital and 1 acquired as a result of trauma. In the 7 cases in the scalp, the arterial supply was traced to the middle meningeal artery. In 1, the branches came through the parietal foramina; in the other 6, numerous arterial branches penetrated the bone. In 3 the aneurysm was demonstrated in the brain at operation, and in 2 other patients in whom the brain was not exposed, intracranial involvement was believed to be present; all of these patients had hemianopsia. Convulsions were present in 4.

Radiographic studies showing dilated arterial paths may be important. Intracranial calcifications are especially important as proving intracranial involvement.

The safest treatment is extirpation of the central mass, which causes disappearance of the external pulsating veins. Injections, although more dangerous, sometimes lead to good results and are to be preferred in some cases, as when the scar would be disfiguring. In the presence of intracranial involvement, their use is especially hazardous. Ligation of the external (not the common) carotid is usually unnecessary, although it may be required in occasional cases. Ligation of the arteries of the scalp is useless.

LEWIS G. JACOBS, M.D.

Pneumosinus Dilatans. Hans Brunner, Irwin G. Spiesman, and John J. Theobald. Ann. Otol., Rhin. & Laryng. **54:** 763-785, December 1945.

Pneumosinus dilatans, a pneumatocele of the paranasal sinuses characterized by dilatation of the involved sinus with air, was described by Benjamins in 1918 (Acta otolaryng. **1:** 412, 1918). The authors briefly summarize Benjamins' case and other cases to which he referred, describe the essential features of several examples from the subsequent literature, and present four new cases. The first of their own series they consider a perfect example of the condition which is referred to as "pneumosinus frontalis dilatans." It demonstrates the slowly growing tumors over both eyebrows, the moderate degree of headache, the huge frontal sinuses, the walls of which are thin and without obvious defect, the absence of fluid in the sinuses, and the obstruction of the nasofrontal duct. The patient was operated upon but the result was unsatisfactory. Certain acromegalic features were present, and x-ray studies eventually revealed enlargement of the sella turcica and partial destruction of the posterior clinoid processes, leading to a diagnosis of adenoma of the hypophysis and incipient acromegaly.

In the three other cases recorded, involving the right maxillary and sphenoid sinuses, the right maxillary sinus, and the ethmoid sinus, respectively, there were also bony changes affecting the walls of the dilated sinuses, due to a focal osteitis in two instances and probably to an old fracture in the third.

From an analysis of this group of cases, the authors conclude that in certain alterations of the bone the sinuses become dilated on account of the bone disease. Why some alterations of the bone, such as osteitis deformans, generalized osteitis fibrosa or leontiasis ossea, usually cause an obliteration of the sinuses while other alterations cause the opposite finding, it is not possible to explain fully. The time when the bone alteration sets in would seem, however, to play a role. If the disease begins at a time when the paranasal sinuses are developed, it may narrow the sinuses provided the disease is not destructive, but productive, in character. *If the bone alteration begins at a time when the sinuses are not yet developed*, as was true in the cases reported, the result may be an absence or a dilatation of the sinus. The latter finding is obtained in acromegaly, focal osteitis fibrosa, and fractures, while an osteomyelitis, for example, usually prevents the formation of a paranasal sinus.

Pneumosinus dilatans is thus not a morbid entity but a symptom of a skeletal disease, which may be focal or systemic in character. The dilatation of the sinuses is bilateral when the bone alteration is systemic, as in acromegaly; unilateral when the bone alteration is unilateral, as in focal osteitis or fracture.

STEPHEN N. TAGER, M.D.

THE CHEST

Anatomy of the Blood Vessels of the Human Lung as Applied to Chest Radiology. Thomas Lodge. Brit. J. Radiol. **19:** 1–13, January 1946.

For this study of the anatomy of the pulmonary vessels, three methods were used, celloidin models prepared by the corrosion technic, radiography following injection of the vessels with barium sulfate suspension, and tomography on living subjects.

There is a basic pattern of the blood vessels of the lungs, in general following the bronchial distribution. The relations of the artery, bronchus, and vein described by Greineder's law (artery, bronchus, and vein are found in that order, proceeding counter-clockwise in the right lung and clockwise in the left lung) were confirmed. Except in the upper lobes, variations from this basic pattern are uncommon, though there may be duplications, *i.e.*, two parallel vessels instead of one. In the upper lobes, two variations are commonly found, one in which the vessels come from a main trunk like the branches of a tree, the other in which the branches arise from a common basic vessel like the stems of a bush.

After proceeding obliquely upward for a short distance, the right upper lobe artery divides into three branches: the apical, which goes upward and outward toward the apex; the axillary, which may be oblique or almost horizontal; the pectoral, which passes forward horizontally to the anterior and lowest portion of the

lobe. There are four main veins which drain the areas indicated by their names: subpleural mediastinal, apical, pectoral, and axillary. (The terminology used is chiefly that of Ewart for the arteries and Herrnheiser for the veins.)

The right pulmonary artery, continuing as the intermediate artery, gives off (1) a middle descending trunk, the lower lobe artery; (2) a posterior horizontal trunk which passes upward, outward, and backward to the apical portion of the right lower lobe; (3) an anterior and medial trunk, the right middle lobe artery. Soon after entering the lobe, the right middle lobe artery divides into two branches, the sternocardiac and the superficial mammary cardiac. There are two chief veins in the right middle lobe, the paramediastinal and the costal.

The lower lobe artery proceeds downward, outward, and slightly backward, becoming external to the lower lobe bronchus, and gives off the retrocardiac, anterior basal, axillary basal, and posterior basal arteries. The last lies posterior to its bronchus. The veins of the right lower lobe are not well standardized. In general, there are five, named for the location they drain: apicohorizontal, anterior basal, anterior axillary basal, posterior basal, and posterior axillo-basal. They proceed upward and inward, uniting to form the inferior pulmonary vein.

The vessels of the left lung are homologous to those of the right, with the lingular portion of the upper lobe corresponding to the right middle lobe. There is more variation in the arteries of the left upper lobe. Frequently there are only three, a pectori-apical, axillary, and lingular. The veins follow the same pattern as the arteries.

These vessels may be demonstrated by tomography down to the second branchings if care is used in positioning and "contrasty" films are produced.

SYDNEY J. HAWLEY, M.D.

Respiratory Malformations: Types, Causes and Significance. A Preliminary Report. Hovey Jordan. Am. Rev. Tuberc. **53:** 56–70, January 1946.

Structural anomalies of the respiratory system may be divided into two major groups: (1) those which are connected with or are a part of the respiratory system, such as abnormal fissures or lobes of the lung itself and agenesis of a lung; (2) those having no morphological connection with the respiratory system. Anomalies of this latter group may be further divided into two subgroups. One of these includes anomalous lobes which are attached by a peduncle to some non-respiratory organ or structure, as the posterior mediastinum, diaphragm, etc.; the other comprises anomalous respiratory tissue, more or less cystic in nature, incorporated in the wall of a non-respiratory organ. This type might be considered by some as belonging to the general group of "bronchogenic cysts" but the author prefers to limit the latter term to cysts having a more or less complete connection with the respiratory system and thus more subject to disease.

Two cases of anomalous lobes without connection with the respiratory system are described. The various theories as to the cause for such anomalies are discussed in some detail. The theory of independent evagination of the anlage of the anomaly from the early embryonic gut, because of its faulty differentiation into respiratory instead of gut tissue at the site of evagination, seems to the author to be the most likely explanation.

Considering all types of respiratory malformations, including such variations as azygos and inferior accessory lobes, it is believed that the incidence is about 1 or 2 per cent in the general population. The possibility of disease occurring in an anomalous structure is no greater than in normal lung, and in such structures not connected to the respiratory system it is less.

L. W. PAUL, M.D.

Bronchial Obstruction in Infants and Children. Paul H. Holinger and Ralph G. Rigby. M. Clin. North America **30:** 105–119, January 1946.

The presentation of 3 cases illustrating the basic forms of bronchial obstruction is followed by a general discussion of the symptomatology and physical findings.

The roentgen diagnosis of bronchial obstruction depends upon complete study of the chest. The practice of basing an interpretation on one or two views leads to gross errors not only regarding the presence or absence of an obstruction but also the location of the lesion. Fluoroscopically, areas of density or emphysema, the motion of the diaphragm, and the shifting position of the heart and mediastinum on inspiration and expiration are significant. There are no actual roentgen findings in the by-pass type of valve obstruction, unless the obstructing element is an opaque object. In bronchial obstruction of the check- or ball-valve type the fluoroscopic study is of the greatest importance. It demonstrates an increase in the transparency of the affected lung, a depression and limitation of motion of the diaphragm on the involved side, a displacement of the heart and mediastinal structures toward the uninvolved side on expiration, and finally a compensatory increase in the motion of the diaphragm on the uninvolved side.

Obstructive emphysema may be recorded on the roentgenogram by making exposures at extremes of the respiratory cycle and comparing the position of the diaphragm and mediastinum as well as the density of the lungs on the two exposures. In complete obstruction, the roentgen findings are more obvious because of the area of density distal to the obstruction. When the main bronchi are completely obstructed, the heart and mediastinal structures are shifted toward the involved side during both phases of respiration, and the diaphragm is elevated and fixed on that side, with density of the atelectatic lung. Complete obstructions of bronchi leading to single lobes or parts of lobes have less influence on the heart and mediastinal structures, although they usually give roentgen evidence of a shift of these structures toward the involved side, thus aiding in the differentiation between an atelectasis, a pneumonic consolidation, and a drowned lung. Atelectatic lobes or parts of lobes generally assume a more or less triangular shape and are frequently designated as triangular shadows, the bronchial obstruction generally lying at the apex of the triangle. It is essential, however, that the shadow be studied roentgenographically in two planes to localize accurately the particular obstructed bronchus.

"Tuberculous" Bronchitis. Hanns Alexander. Schweiz. med. Wchnschr. **76:** 47–50, Jan. 19, 1946.

Bronchitis occurring in a tuberculous patient is not necessarily tuberculous. With care the true tuberculous type can be distinguished, which is desirable from a therapeutic standpoint.

Recurrent "associated" bronchitis is an accompaniment of an active exudative tuberculosis. It is more common in women, especially in the premenstrual period. It is thought to be due to the development of new pulmonary foci which produce a hyperemia with narrowing of the bronchi. This in turn predisposes to activation of the non-specific catarrhal bronchial infection which accompanies almost all cases of tuberculosis. Therapy includes general measures, a climate without sharp changes, expectorants (never narcotics!), etc.

Allergic bronchitis is paroxysmal. It has been described as "eosinophilic bronchial catarrh." Often it precedes the tuberculosis, and it may be accompanied by asthma. The sputum usually contains eosinophils, and a high eosinophil count in the blood is even more common. Inspiratory and expiratory squeaks and groans may be heard over the chest. The onset may be sudden. Treatment is the same as for asthma.

Stasis bronchitis may be associated with tuberculosis as a result of the circulatory changes secondary to the disease. Diagnosis depends on the demonstration of a right heart failure; the condition improves strikingly following improvement in the circulation.

True bronchial tuberculosis, especially involving the bronchioles, is not uncommon; it may even push the parenchymal changes into the background. An outstanding characteristic is its tendency to produce focal atelectasis. Differentiation is important for prognosis and determination of the proper type of therapy. Pneumothorax is often the cause of massive collapse of the lung, with permanent atelectasis of a part or all. Thoracoplasty often leads to bronchial dissemination. The author has used gold therapy with some success.

A picture similar to tuberculous bronchitis may be the result of a post-tuberculous bronchiectasis, which leads to a chronic, recurrent bronchial catarrh.

LEWIS G. JACOBS, M.D.

Early Diagnosis of Minimal Pulmonary Tuberculosis. I. D. Bobrowitz and Ralph E. Dwork. New England J. Med. **234:** 10–14, Jan. 3, 1946.

The authors studied 200 cases of minimal pulmonary tuberculosis (consecutive sanatorium admissions). Sixty-seven of the group had had some contact with the disease, and the importance of x-ray examination of all persons in contact with tuberculous patients is stressed. All but 37 of the 200 patients had symptoms—cough, expectoration, loss of weight, weakness, fever, hemoptysis, night sweats, streaking, dyspnea, anorexia, chills, hoarseness, and lesser complaints. While there is no characteristic or specific symptom of tuberculosis, any of the complaints listed should suggest the possibility of the disease and lead to x-ray examination of the chest. Râles are the most important diagnostic physical finding but were present in only 57 of these minimal cases. In 156 patients no tubercle bacilli were recovered from the sputum or gastric contents. Thus, while the demonstration of bacilli is proof positive of infection, their absence is not to be taken as excluding it. Repeated examinations are desirable, but it is not necessary to wait for a positive specimen before making a diagnosis, since early x-ray examination will indicate the disease.

X-ray examination was the chief method of diagnosis in this series, having been done in 187 of the 200 cases. In 97 it was employed to confirm suspected tuberculosis, and in 90 a routine examination led to the discovery of the disease. "Certainly," the authors say, "in over 99 per cent of minimal cases it can effect the diagnosis, often long before other clinical or laboratory findings have indicated the disease. No lung examination can be considered complete without an x-ray examination, and a patient should never be told that tuberculosis is absent unless one has been done. This procedure should be employed in every patient with any symptoms suggestive of tuberculosis, in any illness that tuberculosis may simulate, and periodically in all contact cases." By x-ray examination the authors mean radiography. They mention fluoroscopy, but consider it "an imperfect diagnostic method."

JOHN B. MCANENY, M.D.

Tuberculous Cavities and Pneumoperitoneum. N. C. Browne and F. L. Corrigan. Irish J. M. Sc., December 1945, pp. 697–702.

The authors base their approach to the treatment of pulmonary tuberculosis on the premise that in a large percentage of cases a tuberculous cavity means the death of the patient in a relatively short time. Almost invariably it is a post-primary manifestation of the disease.

Following the deposition of the tubercle bacillus, there is tissue destruction and ulcer formation. The subsequent development of this ulcer is conditioned by the concentric elastic pull of the surrounding tissue; the continuously changing subatmospheric intrapleural negative pressure associated with respiratory movement; the fact that, as a result of interaction of tissue destruction and elastic tension, one or more bronchi of progressively larger size communicate with the ulcer, which is evacuated of its content. The combined action of the first two factors produces a gradual though limited enlargement of the ulcer. The first line of active treatment has been based on a neutralization of these two forces and is achieved ideally in a selective artificial pneumothorax, whereby both reduction of respiratory movement and concentric relaxation of the lung are effected. Despite treatment, however, some cavities remain open. The authors believe that their persistence is due to the presence of an unchanged condition of partial bronchial stenosis.

Pneumoperitoneum not only brings about relaxation by the reduction of the hemithorax in an apicocaudal direction, but converts the partial bronchial stenosis into a complete block by compressing and kinking the bronchus leading to the cavity. As shown by Coryllos (J. A. M. A. **100:** 480, 1933), concentric relaxation around a patent tuberculous cavity where there is complete block of the draining bronchus will be followed by air absorption and cavity closure. The present writers have found pneumoperitoneum to be a technically simple, easily reversible, and uncomplicated procedure which can be of definite value in lesions situated in the base or mid-zone of either lung; in the treatment of otherwise uncontrollable hemoptysis "by increasing the rise obtained by a phrenic crush;" to provide apicocaudal relaxation in cases of inoperable apical adhesions in artificial pneumothorax when a major operation is contraindicated; in the treatment of potential artificial pneumothorax in cases too toxic for immediate collapse. Apical cavities have not responded well to pneumoperitoneum, though an improvement is usually seen with reduction in the size of the cavity. The technic of the procedure and its possible complications are described.

From a radiographic standpoint, several observations are made. There is some cardiac distortion, more marked in a left pneumoperitoneum. The liver swings downward toward the middle line, and the gas bubble in the stomach is no longer seen. The spleen is often well outlined. When the sputum is persistently positive over a reasonable period of time, an overpenetrated roentgenogram is desirable, as a patent cavity may be seen to have been pushed up behind the heart. Fluoroscopic examination shows the air bubble to travel around the abdomen with movement of the patient, always occupying the highest point of the abdominal cavity. On lateral fluoroscopic examination, the major portion of the movement of the descending bubble of air under the diaphragm on inspiration is accommodated by forward bulging of the anterior abdominal wall. A corset or tight binder may be used to support a flaccid abdomen to some extent and prevent this excessive bulging.

The authors have used pneumoperitoneum in 45 cases but, as indicated above, they consider its value limited and believe it is unlikely to replace pneumothorax, especially in the treatment of apical and upper mid-lung cavities. In their own cases conversion to artificial pneumothorax was attempted wherever possible, and they believe that selective artificial pneumothorax is still the most desirable form of pulmonary collapse. BERNARD S. KALAYJIAN, M.D.

Results of a Random Chest X-ray Survey of Healthy Troops in Canada. R. W. Boyd. Canad. M. A. J. **54:** 16–19, January 1946.

In order to estimate the incidence of early tuberculosis and to forecast the number of cases of tuberculosis arising among troops in Canada on demobilization, a spot x-ray survey was made of healthy military personnel serving in Canada. More than 5,000 soldiers were selected for this study. The soldiers were all under thirty-five years of age and had all served in Canada continuously for eighteen months or more. None of these had received a chest x-ray examination during this eighteen-month period. The individuals were chosen at random from the various units scattered over Canada. Single 14 × 17-inch films were made, and were interpreted by local military radiologists and were again reviewed by one radiologist at National Defense Headquarters.

Three cases of active pulmonary tuberculosis were discovered, and in 8 cases the findings were suspicious of minimal tuberculosis. Of the 8 suspects, 4 were found to have no disease after four months follow-up and 4 were continued on periodic observation. Twenty-eight men had fibrotic or semicalcified lesions which had been present at enlistment and showed no change. Six others had similar fibrotic changes which showed resolution or healing. Fifty-nine had gross hilar or parenchymal calcifications. One had subacute nontuberculous pleurisy. One hundred and fourteen had some pleural thickening, not of clinical significance. Two had progressive heart disease. Four had atypical pneumonia or basilar infection. One had spontaneous pneumothorax. One had eventration of the diaphragm, and two had residual lipiodol in the lung fields.

Of the three cases of active tuberculosis, 2 were moderately advanced, with cavity formation; the third was minimal.

If the findings of the random survey are applicable to incidence of hidden or unrecognized tuberculosis of the army in Canada, a rate of considerably less than one per thousand may be arrived at. The findings of the routine random survey indicate the value of re-surveying "normal" individuals at periodic intervals.

BERNARD S. KALAYJIAN, M.D.

Annular Areas of Pulmonary Rarefaction in Children. Eileen Phillips and Chester A. Stewart. New Orleans M. & S. J. **98:** 247–252, December 1945.

Because of increasing use of the x-ray, pulmonary cysts and cyst-like areas of rarefaction are being discovered with increasing frequency. These changes may be congenital in origin or secondary to aspirated foreign bodies, lung abscesses, and partial bronchial obstruction associated with infections of the respiratory tract.

The authors present four cases illustrating some of the difficulties which attend diagnosis, particularly when infection accompanies the presence of cyst-like changes in the lungs of children.

ELLWOOD W. GODFREY M.D.

Roentgenologic Findings in the Lungs of Victims of the Cocoanut Grove Disaster. Maxwell Finland, Max Ritvo, Charles S. Davidson, and Stanley M. Levenson, Am. J. Roentgenol. **55:** 1–15, January 1946.

The report of Schatzki (Ann. Surg. **117:** 841, 1943. Abst. in Radiology **42:** 301, 1944) on the roentgenologic aspects of the pulmonary lesions in the cases from the Cocoanut Grove fire seen in the Massachusetts General Hospital is reviewed. The various types of roentgenographic lesions described by him were: (1) atelectasis, which varied from lobar to lobular (more common), (2) emphysema, lobar and lobular in distribution, occurring along with areas of atelectasis in the same lung, (3) miliary mottling of both lungs with individual lesions measuring 2 to 6 mm. in diameter, observed in 2 fatal cases only, (4) pulmonary edema in the same 2 fatal cases. Infarcts, though seen at autopsy, were not recognized roentgenologically.

The cases upon which the present paper is based were seen in the Boston City Hospital, and the authors have described the clinical features of the series elsewhere. Autopsy findings suggested that the clinical manifestations in the severe cases were the result of varying degrees of obstruction due to the pseudomembrane and the viscid exudate which covered the tracheobronchial tree and often extended down to the small bronchioles. These gave rise to patches of atelectasis in some parts of the lung, while in other parts there were areas of emphysema and dilated bronchi due to trapped air beyond the obstructing lesions.

A fairly close correlation was found to exist between the severity of the respiratory symptoms and the extent of the roentgen changes. The latter were essentially the same as those described by Schatzki. The diffuse miliary type of mottling in large areas of the lung was seen more frequently in the early films. Enlargement of the hilar shadows with accentuated bronchial markings was quite frequent. Emphysema was evidenced by patchy areas of increased radiance. Atelectasis manifested by the various types of density described by Schatzki was seen in most of the positive roentgenograms. In addition, there were several cases in which the findings were interpreted as those of partial atelectasis of most of one lobe or one lung. In some cases there

were elevation of the diaphragm, contraction of the intercostal spaces, and an appreciable though not marked shift of the mediastinal contents to the affected side. Extensive pulmonary edema was not found.

In general, the more extensive roentgenographic lesions had largely cleared before the end of the first week. In a few instances, there was marked fluctuation in both physical and roentgen findings, as might be expected. Follow-up roentgen examinations in inspiration and expiration were done in many of the patients who had moderate or extensive changes in the early roentgenograms. No residual abnormalities were detected roentgenographically in any of these cases six months to two years after the fire.

Several typical cases are reported, with roentgenograms showing the various types of lesions encountered.

CLARENCE E. WEAVER, M.D.

A Study of One Hundred Cases with a Positive Coccidioidin Skin Test. Dumont Clark and John H. Gilmore. Ann. Int. Med. **24:** 40–59, January 1946.

Coccidioidin skin tests were done on 372 patients who had spent some time in the Southwestern United States. One hundred and twenty-five reacted positively. Of the positive reactors, 100 in whom pulmonary lesions were demonstrable roentgenographically were chosen for special study. These patients were also skin-tested with tuberculin.

The lung lesions could be classified as coccidioidomycosis in 34 of the selected patients. Nine of these showed *Coccidioides immitis* organisms in the sputum, 15 had a negative tuberculin skin test, and 10 showed *Coccidioides immitis* in the sputum by smear only, or lesions of coccidioidomycosis elsewhere than in the lungs. The pulmonary lesions in the remaining 66 patients who had a positive skin test for both coccidioidin and tuberculin were evaluated in the light of the experience with the known positive cases. Although a definite statement cannot be made, the evidence indicated that the lesions in 36 of these cases were due to coccidioidomycosis.

The organism enters the body through the inhalation of infected dust, or rarely through a skin lesion. The vast majority of infections are mild, self-limited, and involve the lung and associated mediastinal lymph nodes. As resistance to the disease develops, antibodies appear in the blood and the lesion heals. Occasionally fibrosis sets in and a rounded or linear scar remains. In such instances a solid immunity to the disease results. In an exceptional case an abscess may form in the lung or pleura. Rarely the infection enters the blood stream and proves fatal.

From a roentgenographic standpoint, the initial lesion in coccidioidomycosis is a pneumonia-like area of increased density in the lung, of variable size and location. Shortly thereafter, one or both hilar regions usually show evidence of lymph node enlargement, a feature which serves to exclude the superinfection (adult) type of tuberculosis. If the disease does not disseminate, the pneumonia-like area will regress in a period of weeks or months. Frequently this initial lesion is confused with so-called atypical or virus pneumonia. As healing takes place, the lesion may disappear or remain unchanged. If not, a rounded nodular dense area or strand-like area, which often extends into the hilus, is left. Occasionally the nodular lesions show a central area of lesser density which gives the appearance of a cavity.

There were 4 fatal cases in the authors' series. All showed roentgen findings in the chest suggestive of a diffuse inflammatory process. In all the hilar markings were exaggerated, far more so than in the usual inflammations of pulmonary structures. Autopsies revealed enlarged hilar lymph nodes in each instance. The microscopic examination showed the nodes to be involved by coccidioidal granulomata. One patient, just prior to death, presented evidence of a beginning effusion between the right upper and middle lobes. At autopsy a right hydrothorax was present.

STEPHEN N. TAGER, M.D.

Pulmonary Changes in Carbon Tetrachloride Poisoning. Charles Moreau Thompson. Am. J. Roentgenol. **55:** 16–19, January 1946.

Recently a series of 20 cases of carbon tetrachloride poisoning were treated at a Naval Dispensary. Three of the patients were critically ill, and one died. Pulmonary roentgenographic changes were discovered late in the course of events. The changes varied from consolidation of all five lobes to mild increase in lung markings. One case showed a change in the configuration of the cardiac shadow between examinations. Enlarged hilar shadows and peribronchial infiltration were also noted. The amount of change on the roentgenograms of the chest was directly proportional to the severity of the clinical illness. This may be of value as a criterion in individual prognosis. The four more serious cases are described. These presented a toxic nephrotic syndrome with puffiness of soft tissue of the face, hands, and feet. CLARENCE E. WEAVER, M.D.

Streptococcal Miliary Infiltration of the Lungs, with Description of a Case. Philip Ellman. Brit. M. J. **1:** 127–128, Jan. 26, 1946.

A case is reported in which x-ray examination of the chest in a patient with achlorhydric anemia showed diffuse miliary infiltration of the lungs, simulating miliary tuberculosis. The sputum yielded a heavy growth of hemolytic streptococci and the response to penicillin was prompt, the infiltration resolving completely in ten days.

Calcification of the Left Auricle. Report of a Case. A. C. Begg. New Zealand M. J. **44:** 315–319, December 1945.

Calcification in the walls of the left auricle is a rare observation. The author knows of but a single case, beside his own, in which such calcification was demonstrated during life. An illustration of that case appears in "A Text Book of X-Ray Diagnosis" by British Authors (edited by Shanks, Kerley, and Twining, London, H. K. Lewis & Co.) but no clinical details are given in connection with it except that the patient suffered from mitral stenosis.

The author's patient was a woman of sixty-one, admitted with acute bronchitis and extreme cyanosis. At the age of thirty-one, she had been told that she had a "leaking valve" in her heart and had been advised to live quietly. She continued an active life, however, up to seven years prior to admission, when she first began to experience dyspnea on exertion and some cyanosis. She had had several attacks of unconsciousness, with convulsions, in the past five years and, since the first of these, had been taking digitalis regularly. Examination showed marked cyanosis about the lips, ears, and extremities. The pulse was irregular in rate and

force—about seventy beats a minute. The blood pressure was 190/120. The apex beat was in the seventh interspace, 5 1/2 inches to the left of the midline, and the right border of the heart was 1/2 inch beyond the right edge of the sternum. Numerous systolic and diastolic murmurs were present. The electrocardiogram showed evidence of auricular fibrillation and a tendency toward right axis deviation. The clinical findings suggested the likelihood of stenosis and regurgitation of both the mitral and aortic valves. Although a history of rheumatism could not be elicited, that was thought to be the probable etiologic factor.

On fluoroscopy, the heart shadow was greatly enlarged, both to the right and left. The left auricle with its appendix could be clearly outlined because of the deposits of calcium within its walls. It was greatly enlarged. The inferior surface moved downward on ventricular systole but no intrinsic auricular contraction could be seen. There was definite calcification of the leaves of the mitral valve which could be seen with the characteristic dancing movement. The aortic pulsation was normal. Enlargement of the pulmonary artery shadow was noted.

Radiographic study showed the area of the heart to be about two and one-half times that predicted for a woman of the patient's height and weight. It was estimated that the heart volume was 1,800 c.c. The left ventricle and the right ventricle were both considerably enlarged. The calcium deposits in the left auricle appeared to involve its entire surface, including the appendix and the interauricular septum. The calcification was most marked posteriorly and least marked in the vicinity of the mitral valve and interauricular septum. The capacity of the left auricle was estimated at 250 c.c., compared to a normal of 30 to 45 c.c. The illustrations included with the article are of unusual interest in showing the relationship of the left auricle to the rest of the heart shadow and to the surrounding structures, with particular attention drawn to the deviation of the esophagus and the distortion of the left main bronchus produced by the enlarged left auricle.

Heavy deposits of calcium were present in the mitral valve, the position of which could readily be seen in all projections. Calcification was also present in the region of the aortic valve, but the deposits were lighter and this valve could not be clearly demonstrated fluoroscopically. Exposures of 1/10 second with a Potter-Bucky diaphragm were most satisfactory.

It would appear that the primary lesion in this case was a stenosis of the mitral valve which had led to chronic enlargement of the left auricle and subsequent auricular fibrillation. Satisfactory compensation of the right heart enabled the patient to lead an active life without symptoms of cardiac distress. During this time, calcium was deposited in the walls of the dilated left auricle and in the mitral valve as a degenerative change. As this gradually increased, mitral incompetence increased, with subsequent enlargement of the left ventricle. These gross changes in cardiac dynamics, however, affected the patient very little until the right ventricle began to fail with the additional load of a respiratory infection.

The patient gradually improved and was discharged from the hospital five weeks after admission. She was able to be up and about without dyspnea though she was still somewhat cyanotic.

BERNARD S. KALAYJIAN, M.D.

THE DIGESTIVE SYSTEM

Lymphosarcoma, with Primary Manifestations in the Gastrointestinal Tract: Report of Seven Cases Studied Roentgenologically. Robert D. Moreton. Texas State J. Med. **41:** 458–464, January 1946.

From a pathologic standpoint, gastro-intestinal lymphosarcoma and carcinoma differ from each other in that the former arises in the lymphoid tissue of the submucosa and infiltrates the mucosa and muscularis, whereas the latter has its origin in the mucosa. Ulceration, when it occurs, is thought by some to be due to necrosis from pressure and loss of blood supply rather than to the malignant invasion itself. Lymphosarcoma may produce an intrinsic, extrinsic, or infiltrating type of lesion. The intrinsic type may manifest itself as single or multiple polypoid growth protruding into the intestinal lumen and producing obstructive symptoms. The infiltrating or intramural type produces an annular lesion which may involve one or more segments of bowel. This type of growth forms, at times, an annular cuff in the involved portion and produces symptoms of incomplete obstruction.

Roentgen findings are not sufficiently characteristic to warrant a specific diagnosis of lymphosarcoma of the gastro-intestinal tract, but it has been suggested that the possibility of gastric lymphosarcoma be considered in all atypical cases showing carcinoma-like deformities. The roentgen findings in the stomach may be negative in the very early stages. In other cases the roentgen report may be gastric ulcer, diffuse infiltration of the entire stomach with or without prominent rugal markings and with or without peristaltic variation, polypoid lesions indistinguishable from carcinoma, or simply an obstructing lesion of undetermined type at the pyloric end of the stomach. In the small bowel, the lower portion of the ileum is the most common site of involvement. Many variations in the roentgen appearance occur. There may be patchy, diffuse, irregular distribution of the barium or a diffuse thickening and contraction deformity as seen in hyperplastic enteritis. Other findings may be those of obstruction, entero-enteral or entero-colic intussusception, or of a simple deficiency state. In the colon, the lesions may be polypoid; there may be filling defects resembling carcinoma, or intussusception of the colocolic type, or rarely diffuse infiltration of the bowel.

Since sarcomas of all types constitute only 3 per cent of malignant growths of the gastro-intestinal tract, to risk a definite diagnosis of gastro-intestinal lymphosarcoma would obviously be somewhat hazardous. Despite this, roentgen examination is indispensable for discovering and localizing the lesion, determining in most instances its neoplastic nature, and permanently recording the original involvement for the determination of its progress or regression at subsequent examinations.

Reports of 7 cases are presented, in which the diagnosis was established either by exploratory operation or removal of enlarged lymph nodes. One patient had lesions in the terminal portion of the ileum and the cecum. In one the stomach and cecum were involved. Two had polypoid lesions in the stomach. A fifth had involvement of the distal portion of the ileum for about 50 cm. A relatively small segment of the ileum and the distal half of the stomach, respectively, were involved in the two remaining cases. An exploratory operation was done in each of the cases and 5 patients

received postoperative roentgen therapy. There were five deaths in the series. Two patients, with involvement of the stomach, showed no evidence of recurrence when last seen, thirty-four and thirty-six months after their first admission. One of these patients had been treated by resection and postoperative irradiation; the other by irradiation alone.

The author suggests that the term "tumefactive lesion" rather than carcinoma should be used in radiologic and gross pathologic diagnosis of gastro-intestinal neoplasms, since it carries no etiologic or histologic implication. BERNARD S. KALAYJIAN, M.D.

Gastric Carcinoma: Review of Errors in Diagnosis. Meyer Golob. Am. J. Digest. Dis. **13:** 17–23, January 1946.

The author lists four factors which enter largely into the wrong interpretation of symptoms and lead to delay in the diagnosis of gastric cancer: (1) age incidence; (2) length of history; (3) size or site of lesion; (4) malignant degeneration of a benign ulcer. Neither the age of the patient, the size of the lesion, nor the presence of hyperchlorhydria or achlorhydria should lessen the suspicion of gastric cancer. Nor should dependence be placed on a therapeutic test, since practically every case shows relief of symptoms when clinically treated.

To illustrate the fallacy of ruling out cancer because the patient is "too young," a case is recorded in a man of 37 with a history of gastric symptoms for eight years. He was first seen by the author in January 1936, with complaints dating back two years—loss of weight, anorexia, and hypochlorhydria progressing to achylia. Roentgen examination in December 1934 had shown an irregular antrum and bulb which were thought to be due to an old ulcer. Exploration was recommended, but the patient improved on a medical regime, and operation was postponed until January 1936, when an anaplastic grade IV carcinoma was found, with metastases in the regional lymph nodes.

Two cases are presented to show that a short history does not necessarily rule out cancer. The first patient, a 64-year-old man, showed the textbook picture of malignant neoplasm, though earlier roentgen examination in a commercial laboratory had been reported negative. The second patient, a man of 45, had symptoms of three months' duration, mimicking duodenal ulcer. At operation a huge ulcerating cancer of the stomach was found.

The gastric chemistry may also be misleading, as shown by a case in a patient of 31 with symptoms of seven months' duration but no abnormal chemical findings. Roentgen examination showed a slightly deformed duodenal cap and a serrated defect on the greater curvature. The case was diagnosed as duodenal ulcer and a Sippy diet was given for a year. Roentgen examination at the end of that time revealed the same defect, and laparotomy showed advanced cancer.

In another case, in a neurotic woman of 52, with a long history of gastric disturbances and a positive test for occult blood in the gastric contents, an unusually small defect on the lesser curvature was ignored for more than a year, during which the patient was treated for gastritis. At operation a far advanced carcinoma was found.

That misleading roentgen findings may obscure the transitional phase of a benign gastric ulcer into a malignant neoplasm is shown by the case of a man aged 55 who had a gastric ulcer for twenty years. Repeated roentgen examinations showed the ulcer to have become smaller. The patient died from hemorrhage, and autopsy showed a malignant ulcer with metastasis. In discussing this case the author quotes Alvarez as stating that, "the only way in which one can hope to cure cancer of the stomach is to excise it during the stage in which it looks and behaves like a benign ulcer." A lesion of the stomach which is apparently healing, as shown by roentgen examinations, may actually be malignant and infiltration of tissue at the base of the defect may occur while the cancer is spreading and give the impression that the niche is filling up.

JOSEPH T. DANZER, M.D.

Diverticula of the Stomach. W. R. Moses. Arch. Surg. **52:** 59–65, January 1946.

Diverticulosis of the stomach is an uncommon lesion, generally found on the posterior wall near the lesser curvature in the cardia. It is frequently without symptoms, and when present, these are not characteristic. In about 30 per cent of the cases other gastroduodenal disease coexists and produces symptoms, and in about a third the symptoms are due to the diverticulum itself.

Diverticula may be classified as true (congenital) and false (acquired). The latter may be further divided into traction and pulsion types.

The roentgenologic differentiation of a diverticulum from a pentrating ulcer is based on the following points. In ulcer there is a tendency to spasm near and opposite the lesion and infiltration or rigidity of the mucosal border is present. In differentiating from diaphragmatic hernia, it is helpful to note that diverticula are larger on expiration, herniae on inspiration. The presence of an intrathoracic shadow and the constriction of the neck at the passage through the diaphragm are also indicative of hernia. Gastroscopic examination is an important aid, but the diagnosis may easily be missed by any method. If treatment is indicated to control symptoms, surgery is probably the method of choice.

A case, in which rupture of a gastric diverticulum led to intraperitoneal hemorrhage, diagnosed at operation, is reported. This complication has not previously been recorded. LEWIS G. JACOBS, M.D.

Diverticula of the Colon versus Gallstones. Arnold Galambos and Wilma Mittelmann-Galambos. Am. J Digest. Dis. **13:** 14–16, January 1946.

A case of diverticulosis is presented in which the diverticula were confined to so circumscribed an area around the hepatic flexure that roentgenologically they were at first mistaken for gallstones. They even appeared to be facetted, while some had a dense cortex suggestive of calcium-containing calculi. It was later found that the resemblance to stones was due to residual barium following a barium enema study. The diverticula had not filled at the time of the enema, nor were they shown on a film made after evacuation. They were seen, however, during cholecystographic study, when a non-functioning gallbladder was demonstrated. A subsequent film showed some of the pseudo-stones to have become smaller and others to have disappeared and this led to the correct interpretation.

JOSEPH T. DANZER, M.D.

Appendicitis with a Massive Peristaltic Movement of the Colon. (Case Examined by Barium Meal and by Enema.) J. A. Mathez. J. de radiol. et d'électrol. **26:** 364–368, 1944–45.

A girl of twenty-five came under observation because of chronic abdominal distress and was examined by barium meal and enema. She evidently had chronic appendiceal involvement and exhibited tenderness over the cecum. When the examiner was palpating that area, the right half of the colon contracted. This occurred several times and, though more barium was admitted, the cecum tended to remain empty.

The author discusses this phenomenon academically, quoting some of the earlier German roentgenologists who spent a great deal of time in deciding by what sort of movement the large intestine emptied itself. He concludes that the patient's having appendicitis probably had something to do with the "*grand mouvement*" upon which he dwells at such length, which is tantamount to an admission of entire unawareness of the modern approaches to gastroenterology. The cecum may, of course, be irritable in appendicitis; and in regional enteritis, too, and in carcinoma of the cecum.

PERCY J. DELANO, M.D.

Retroperitoneal (Mesenteric Pouch) Hernia. Case Report. I. S. Ravdin and Philip J. Hodes. Ann. Surg. **123:** 106–110, January 1946.

The authors report a case of retroperitoneal hernia containing a giant Meckel's diverticulum, associated with recurrent bouts of intestinal obstruction. The diagnosis was suggested from the radiographic finding of an air and fluid level in a dilated loop of gut in the right upper quadrant. A small intestinal study revealed the gas-filled loop to be distal ileum, while lack of mobility on manipulation and positioning strongly suggested that the loop was enclosed in a membrane or sac. These findings were confirmed at operation. Only a limited portion of the ileum was involved, and the hernial sac was avascular, with no large vessels either at the entrance or exit. Following complete resection and anastomosis the patient made a good recovery, with relief of all symptoms. Roentgenograms and photographs are included.

ELLWOOD W. GODFREY, M.D.

Cholecystography for Children. Victor E. Hrdlicka, Carlton G. Watkins, and John A. Robb. Am. J. Dis. Child. **70:** 325–328, November-December 1945.

Cholecystography with Priodax was carried out in 47 unselected infants and children. The medium was found to be satisfactory for those over nine months of age. Under that age the percentage of successful results was low. The recommended dose of 0.5 gm. per 10 kg. of body weight proved adequate for children over four years, but larger dosage—as much as 1.5 gm. per 10 kg.—was sometimes necessary for younger children and infants. Toxic effects were minimal, even in very young infants given two or three times the ordinary dosage of Priodax.

Double Gallbladder. Report of a Case. Warne L. Haight. U. S. Nav. M. Bull. **46:** 117–119, January 1946.

A case of double gallbladder, presumably with separate cystic ducts, is reported. The diagnosis was established by cholecystography.

THE SPLEEN

A Calcified Cyst of the Spleen, Demonstrated Roentgenologically. Erling Kierulf. Acta radiol. **27:** 43–46, Jan. 31, 1946.

The author prefaces the presentation of a case of calcified cyst of the spleen, demonstrated roentgenographically, with a brief description of calcifications in that organ and a classification of splenic cysts.

THE MUSCULOSKELETAL SYSTEM

Normal Development of the Ossific Centres During Infancy and Childhood: A Clinical, Roentgenologic, and Statistical Study. Olle Elgenmark. Acta paediat. **33,** Supplementum I, pp. 1–79, 1946.

In previous studies of the development of ossification centers the practice has generally been to determine their differentiation from observations made on bone development in one area of ossification, usually the hand or the hand and foot. In the present investigation, the author shows that there is no absolute correlation between the appearance of the different ossific centers and that it is consequently not possible to draw hard and fast conclusions concerning other centers on the basis of the differentiation present in a few isolated areas. Not even in the two halves of the body do the corresponding centers make their appearance quite uniformly.

In this study a number of simultaneous observations were made of the dates of appearance of the centers in several readily accessible ossification areas, *i.e.*, the skeleton of both extremities on the right side of the body, comprising 68 ossific centers, and in a few subjects, for purposes of comparison, the corresponding parts of the skeleton on the left side also. Five years was taken as the upper age limit, because only a few centers appear later in these areas. A total of 1,190 observations were made on 852 carefully selected children, and the material was then studied statistically.

The investigation brought out the fact that there is great variation in the times of appearance of the individual ossific centers, and also that there is a considerable difference between the sexes, the centers of girls differentiating much earlier than those of boys. Appropriate calculations proved that there are significant and positive correlations of equal degree between the differentiation of the ossific centers and age, height, and weight. By means of partial correlations between age and height and ossific centers, it was established that in infancy the height shows a stronger correlation with ossific center development than age; later on, the correlation is largely equal.

Tables for the development of ossification centers are presented.

A Study of the Development of Rickets in Premature Infants. Gert v. Sydow. Acta paediat. **33,** Supplementum II, pp. 1–122, 1946.

All premature infants with a birth weight not above 2,000 gm. born at the Sahlgren Hospital, Göteborg, during a two and one-half year period, whose condition permitted, were examined at regular intervals, with blood analyses and roentgenograms of the wrist. To obtain normal values for the blood chemistry as a control, two groups of normal full-term breast-fed infants

were also studied. The following facts were established by this investigation.

Premature infants receiving only human milk without any supplement in the first days of life have about the same serum inorganic phosphorus values as normal, higher serum phosphatase, and lower serum calcium and serum protein values. In the following months, the serum phosphatase increases, and the serum inorganic phosphorus and serum calcium decrease considerably.

Premature infants fed human milk and vitamin D show significantly higher serum calcium than those not receiving vitamin D. Infants given cow's milk but no vitamin D showed significantly lower values for serum phosphatase and higher for serum inorganic phosphorus than those receiving human milk exclusively. Those given cow's milk and vitamin D showed significantly lower values for serum phosphatase and higher for serum inorganic phosphorus and serum calcium than those given only human milk. Supplies of different mineral preparations may act to a certain extent in the same manner as cow's milk. Seasonal variations in the serum values have been established for the normal groups and for premature infants receiving human milk with or without vitamin D.

Roentgen signs of rickets appear in more than half the infants after the first month of life; before the age of one month, they appear occasionally. Metaphyseal decalcification, which may possibly be regarded as an early rachitic or prerachitic sign, usually appears before the age of one month. Except for metaphyseal decalcification, "fringing" and "cortical spurs" seem to be the earliest signs of rickets in premature infants, usually appearing in the first half of the second month. At the appearance of fringing, serum phosphatase is possibly somewhat higher and serum inorganic phosphorus somewhat lower than the average for premature infants. At the appearance of spurs, serum phosphatase is possibly higher than the average, but serum inorganic phosphorus seems to be average.

"Cupping," "spreading," and "periosteal encasements" of the shaft were not very often recorded and were coincident with or even subsequent to calcification at the epiphyseal line. Therefore, in this series, they may be regarded as fairly late signs of rickets.

Calcification at the epiphyseal line was always one of the latest signs of rickets to appear. The serum values at its appearance are not more normal, however, than the mean for the age group, and it may then be regarded as a sign of healing but not of health.

When roentgen signs of rickets are present in premature infants fed human milk with or without vitamin D, the serum phosphatase is much higher and the serum inorganic phosphorus lower than when the roentgen picture is normal. In premature infants fed cow's milk there is no difference in these respects. In those not receiving vitamin D, the serum calcium is much lower when roentgen signs of rickets are present, but when vitamin D is given, serum calcium is the same in infants with rickets and in those with normal roentgen findings.

The author concludes that human milk may not supply the premature infant with a sufficient amount of phosphorus, though it gives a fairly sufficient amount of calcium. The latter, however, will not be absorbed in sufficient amounts unless vitamin D also is given. When cow's milk is supplied, a sufficient amount of phosphorus is absorbed, but not of calcium unless vitamin D is given. Rickets in the first months of life in premature infants is most frequently due to an insufficient supply of phosphorus or an insufficient absorption of calcium, but these may not be the only causes.

Rickets and Infantile Scurvy Occurring in a Case of Osteogenesis Imperfecta. Ralph S. Bromer. Am. J. Roentgenol. **55:** 30–36, January 1946.

Affections of the skeleton may occur simultaneously in children. The author reports the case of a male Negro infant showing evidence of osteogenesis imperfecta, with pathological fractures, in whom rickets developed at the age of three months and infantile scurvy at twenty-one months. The unusual feature of the case was that, though the osteogenesis imperfecta was apparently present from birth, the roentgen changes in the skeleton were characteristic of the late type of the disease rather than the congenital. The case is described in detail and roentgenograms are reproduced showing the typical bone changes of the three diseases.

CLARENCE E. WEAVER, M.D.

Congenital Malformations of the First Thoracic Rib: A Cause of Brachial Neuralgia Which Simulates the Cervical Rib Syndrome. James C. White, M. H. Poppel, and Ralph Adams. Surg., Gynec. & Obst. **81:** 643–659, December 1945.

The authors have observed 10 cases of abnormalities of the first thoracic rib, 5 of which were asymptomatic and 5 of which presented a cervical rib syndrome. The case histories of the latter group are given in detail, and roentgenograms of patients from both groups are reproduced. The literature is reviewed.

The abnormal rib is generally a rudimentary structure terminating in a synostosis or pseudoarthrosis with the second rib near the scalene tubercle, or in a free end in the soft tissues at the base of the neck, which may be connected by a ligamentous band with the manubrium sterni.

From a review of comparative anatomical studies and embryological theories, the authors conclude that these malformations are best explained by errors of body segmentation in early embryonic development and are often brought about by abnormal formation of the brachial plexus and blood vessels. The symptoms and clinical evidence consist of supraclavicular bony prominence, irritation or paralysis of the brachial plexus, and compression of the subclavian vessels as they cross the defective rib.

On the basis of symptoms and physical signs the authors cannot differentiate first rib abnormalities from cervical rib or from compression by the anterior scalene muscle. Even roentgen studies require special care if a correct diagnosis is to be made. It is essential to be able to outline all the vertebrae in the neck and upper thorax on an anteroposterior film which shows the details of the upper rib articulations as well. This can be accomplished by making a long exposure with the patient opening and closing his mouth. In this way the shadow of the mandible is blurred so that it does not obscure the outlines of the atlas and axis. Anteroposterior x-ray films should include the whole of the second as well as the first rib, as the anomaly often involves the two. All of the bony structures bounding the thoracic apex require careful scrutiny. In unusual cases it may be advisable to include the entire spine, so that the total number of ribs and lumbar vertebrae can be counted. Unless these precautions are observed, first rib deformities may be missed.

As to treatment, a trial of conservative measures is recommended. If these are unsuccessful, then exploration and transection of the anterior scalene muscle may be done plus (unless the rib is quite rudimentary) excision of the rib from the clavicle to where the bone disappears in the posterior muscles of the neck.

This is an informative article but it should be noted that it deals with an obviously selected group of patients. The percentage of symptomatic cases would be much lower with a more comprehensive method of selection. FREDERICK A. BAVENDAM, M.D.

A Contribution to the Radiologic Study of the Deficiency Osteopathies: Syndrome of Milkman-Debray-Looser. F. Lepennetier, E. Gilbrin, M. Godefroy, and R. Tricot. J. de radiol. et d'électrol. **26:** 197–209, 1944–45.

The authors describe in great detail a case of the so-called syndrome of Milkman-Debray-Looser, "remarkable for the multiplicity of the bone changes," and make this the occasion for a general discussion of the disease.

As to the lesion itself, little is added to that which has already been written, for, under one title or another, the roentgen appearance has been fully described by various writers over a period of some years. Briefly, it consists in a line of decreased density, occurring more often in long bones but also in flat ones, and with no definite site to which its occurrence can be said to be restricted. In the long bones the line is transverse. From the beginning [and since the first comprehensive description was by Looser, whose name the lesion bore for years, it seems a bit out of keeping that the authors should have contrived a title in which his name forms the last link] the condition has been considered to be of nutritional origin. The variant described by Milkman bore, as part of its title, the word "fracture." One of his publications (Am. J. Roentgenol. **32:** 622, 1934) is headed "Multiple, Symmetrical, Spontaneous Fractures," and this entity became known in America as "Milkman's disease."

After march fracture involving a metatarsal became better understood and passed from the category of idiopathic diseases (Deutschländer's disease, etc.), other sites of similar fracture began to be described: the tibia, neck of the femur, even the pelvis. The similarity of the fracture line seen in these instances with those of the original Looser *Umbauzonen* finally began to be generally appreciated, and gradually the concept of this bony phenomenon is becoming clarified.

The present paper is profusely illustrated; early and late stages of the fracture lines are shown. The history of such injury is, however, as nebulous as traditionally postulated. The description of the lesions is rather redundant. Milkman's modest contribution receives somewhat more stress than would appear indicated. The German contributions have consistently been the closest to pointing out the true state of affairs, with their frequent emphasis on the coincident nutritional state of the individual. [Only in metatarsal march fracture can the constitutional state be set aside; here the predisposing factor is a purely local one—the "weak foot" as originally described by Morton.]

One tries, from time to time, to gather together the rapidly accumulating terms descriptive of a basic pathologic entity, but it is difficult to keep abreast of them. For march fracture, strain fracture, Looser's zones, *Umbauzonen*, transformation zones, acute transverse atrophy of bone, fatigue fracture, multiple idiopathic symmetrical fractures, etc., the term "hunger osteopathy," which was apparently first employed by the German writers, might well be substituted.

PERCY J. DELANO, M.D.

Chronic Sclerosing Osteitis. Henry W. Meyerding. Western J. Surg. **53:** 413–420, December 1945.

The term "chronic sclerosing osteitis" is used to designate those cases of low-grade infection which produce a marked thickening of the bone localized to a single segment. The author's series of 80 cases represents about 2 per cent of all the cases of osteomyelitis seen at the Mayo Clinic in thirty-two years, from 1912 to 1943. Thirty of the number were previously reported by Henderson (J. A. M. A. **82:** 945, 1924).

The outstanding symptom of chronic sclerosing osteitis is persistent pain of varying severity, which may be present for months to years. This pain, as a rule, is worse at night; it usually remains localized, and is deep-seated, along the shaft of the long bones. The average duration of the cases in this series was 1.4 years. Trauma, exposure, and debilitating disease aggravate the pain. The blood findings are usually not of great help, since the white count is commonly normal and the concentration of hemoglobin and the red count are frequently within normal limits. Flocculation tests are negative. The most significant findings are those revealed by radiography. The exact site and size of the lesion can be easily determined. The radiographic appearance is that of a dense sclerotic area in the shaft of the long bone involving the cortex and the spongy bone. There is often a central area of decreased density which is considered the nidus of the infection. The cortex may be involved on one side only, or the involvement may go completely around the cortex and produce considerable enlargement.

The author goes into detail as to the differential diagnosis of this lesion from syphilis, osteogenic sarcoma, osteitis deformans, traumatic ossifying hematoma, Ewing's sarcoma, and metastasis from prostatic carcinoma. Since the details of such a differential diagnosis are well known to most radiologists, they are not included in this review.

The treatment of chronic sclerosing osteitis is surgical, the extent of the operation depending on the degree of involvement present. The author advises saucerization of the involved bone with removal of as much of the infected bone as possible rather than simply drilling the bone. The average age of the patients is twenty-five years, and the end-results of the operative procedure are usually quite good. The author states that about 70 per cent of the patients had complete relief of their symptoms and about 15 per cent had partial relief.

BERNARD S. KALAYJIAN, M.D.

Generalized Leontiasis Ossea. L. H. Garland. Am. J. Roentgenol. **55:** 37–43, January 1946.

Leontiasis ossea is an uncommon disease. The hyperostosis may be limited to one bone of the skull or involve all of them. In the latter event, the bones of the face may be enlarged and distorted, but the facies is almost never leonine. Occasionally there is involvement of the long bones. The disease begins in childhood or adolescence, and females are said to be more commonly afflicted than males. The cause is unknown. Grossly, Knaggs (Inflammatory and Toxic Diseases of Bone. New York, William Wood & Co., 1926)

recognized two types of the disorder, the creeping periostitic and the diffuse osteitic type. Some patients have severe headaches and various visual or auditory disturbances. Exophthalmos is frequently present. Insomnia, mental dullness, and convulsions may develop. The course is variable (from twenty to forty years). The diagnosis is usually made by roentgen examination of the skull, which reveals diffuse hyperostosis of the bones of the face (notably the malar, frontal, and sphenoid bones). The hyperostosis is usually uniform and "osteomatous." Inflammatory osteitis, Paget's disease, and acromegaly are to be differentiated.

A case of generalized leontiasis ossea in a male aged thirty years is reported. Both types of the disease were present in this patient. The cranial bones and mandible showed typical diffuse "osteitic" overgrowth; the long bones of the extremities showed diffuse symmetrical cortical and periosteal overgrowth.

CLARENCE E. WEAVER, M.D.

Mutational Dysostosis (Cleidocranial Dysostosis). A. B. Soule, Jr. J. Bone & Joint Surg. **28:** 81–102, January 1946.

Mutational dysostosis is frequently transmitted from parents to offspring and is characterized by multiple variable developmental skeletal anomalies, usually aplasia of the clavicles, delay in closure of the fontanelles and sutures, brachycephaly, prognathism, irregularity in dentition, and structural abnormalities of the other bones. The skull may show increased transverse and decreased anteroposterior diameters. Some of the bones are underdeveloped. The facial bones are poorly developed and asymmetrical. The teeth will show abnormalities when dentition occurs. Some may be absent or there may be supernumerary teeth.

The clavicles are most commonly abnormal. They may show small defects or be completely absent. The scapulae are small and primitive. Anomalies of the humerus, radius, and ulna are uncommon but do occur.

The spine may show curvatures, fusion defects, and maldevelopment of vertebrae. The pelvic bones are small and primitive in appearance. There may be failure of bones to fuse. The femoral neck may be deformed or absent, otherwise the femora, tibiae, and fibulae are usually normal.

There is a striking resemblance between all these patients in appearance. They are usually in good health and often are led to consult a physician because of the dental abnormalities.

Six cases are presented, with reproductions of radiographs which show various abnormalities.

JOHN B. MCANENY, M.D.

Hemiatrophy of the Body in Adult Life. Norman Reider and Glen S. Player. J. Nerv. & Ment. Dis. **103:** 1–8, January 1946.

The causes of hemiatrophy of the body are numerous, including birth injuries, head trauma in childhood or adult life, encephalitis of various types, vascular lesions, and tumors. None of these factors, however, seems to have been present in the two cases recorded here. In such idiopathic cases, pneumoencephalography offers a means of definite diagnosis.

The authors' two patients were soldiers 22 and 24 years of age. The first had been in excellent health throughout a long combat experience. He was hospitalized for trench foot, and during a routine examination it was noted that the right arm and leg seemed smaller than the left. On questioning, it was learned that there had been a "little tiring" of the right leg during the past three months. The atrophy continued to increase for a month, after which progress ceased. There was a difference of 2 inches in the circumference of the calves, and of 1 1/2 inches in the circumference of the biceps. There was no change in motor power, sensation, co-ordination, or reflexes. A pneumoencephalogram made six months after onset showed slight bilateral internal hydrocephalus, with the left lateral ventricle larger than the right.

The second patient complained of headaches on walking, dull pain, and stiffness of the right leg. A slight difference in the size of the extremities seems to have been noticed previously but received no special attention. Four months later the headaches were worse and the right leg was painful. Four months after this, the patient was thrown from a jeep, following which he had transient diplopia and weakness of the right arm. A difference of 7/8 inch was found between the right and left calves; the reflexes of the right arm were slightly more active than those on the left, and there was a transient right ankle clonus. Further examination showed the face, trunk, and extremities all to be involved in the hemiatrophic process. A pneumoencephalogram revealed dilatation of the left lateral ventricle, especially in its middle portion.

In each of these cases a spinal origin of the muscular atrophy was suspected, but a cerebral origin was established by the encephalogram. The authors believe that the more common phenomenon of facial hemiatrophy would frequently be shown to be cerebral in origin if the possibility were kept in mind and encephalography were done in all cases. They feel that it is possible, also, that the rare atrophies of an extremity attributed to subclinical poliomyelitis may be of cerebral origin.

BERNARD S. KALAYJIAN, M.D.

Osteogenic Sarcoma. II. Roentgenographic Interpretation of Growth Patterns in Bone Sarcoma. Ian MacDonald and John W. Budd. Surg., Gynec. & Obst. **82:** 81–86, January 1946.

The roentgen-ray study of bone tumors, according to the authors, should be interpreted as a reflection of their growth characteristics rather than an indication of tumor types, a kinetic rather than a static concept. The roentgenographic features of a bone tumor at any given time are dependent upon the balance between neoplastic activity (osteolysis) and the degree of cortical or medullary reaction (sclerosis) as well as the absence or extent of ossification and calcification.

The observations presented here were made by careful study of 118 cured cases of bone sarcoma (previously reviewed in Surg., Gynec. & Obst. **77:** 413, 1943. Abst. in Radiology **42:** 524, 1944) and a smaller number of uncured cases from the Registry of Bone Sarcoma of the American College of Surgeons. The expression, "osteogenic sarcoma" is used in this article as a generic term for all sarcomas originating in the connective tissue of bone, including osteosarcoma, chondrosarcoma, and fibrosarcoma.

From this study the authors conclude that the experienced roentgenologist can differentiate between benign and malignant tumors with almost complete accuracy through an interpretation of their growth patterns. A diagnosis of osteogenic sarcoma can be

made with reasonable certainty if there is evidence of a cortical malignant tumor, though further differentiation into tumor types by radiographic methods is highly unreliable.

The salient features of the three connective-tissue sarcomas, as noted in the reviewed material, are presented and illustrated in the form of a diagram. The prognostic importance of differentiating osteogenic sarcoma as to tumor type is stressed, since osteosarcoma is almost uniformly fatal, while fibrosarcoma is much less malignant, with chondrosarcoma occupying a median position. That metastatic carcinoma may simulate perfectly the appearance of primary sarcoma of bone is illustrated by a case of metastatic adenocarcinoma from the prostate gland which was diagnosed by three roentgenologists as "typical osteosarcoma." Microscopic study of open biopsy material, therefore, remains the most essential single diagnostic method in bone tumors and should precede the institution of any therapeutic program. The only notable exception is Ewing's sarcoma, in which a therapeutic test with small doses of x-radiation is of definite diagnostic value.

JOHN H. FREED, M.D.

Sarcoma Complicating Paget's Disease of Bone. Thomas J. Summey and C. Lowry Pressly. Ann. Surg. **123:** 135–153, January 1946.

Three illustrative cases of sarcoma complicating Paget's disease are reported. The authors state that there seems to be a definite relationship between osteitis deformans and sarcomatous change. Coley and Sharp (Arch. Surg. **23:** 918, 1931) stated that in patients with Paget's disease and sarcoma of bone the tumor is invariably in parts of the skeleton showing osteitic changes. von Albertini (Virchows Arch. f. path. Anat. **268:** 259, 1928) described a "presarcomatous change" in the bone marrow of multiple bones in long-standing cases of Paget's disease, and Speed (see Hansen: Tr. West. S. A. (1941) **51:** 59, 1942) suggested that the osteoid tissue of Paget's disease has a lesser chronological age than normal bone and is therefore more subject to malignant change.

The prognosis in sarcoma complicating Paget's disease is extremely grave, as the life expectancy is less by ten months than in uncomplicated osteogenic sarcoma in the same age group. Unlike uncomplicated osteogenic sarcoma, the sarcoma of Paget's disease often involves multiple bones. There is no known cure.

The authors have reviewed the literature and have tabulated all the cases of sarcoma in Paget's disease which they were able to find—a total of 76, including their own. A full bibliography is appended.

ELLWOOD W. GODFREY, M.D.

Osteochondromata of the Pelvic Bones. Ralph K. Ghormley, Henry W. Meyerding, Robert D. Mussey, Jr., and Clarence A. Luckey. J. Bone & Joint Surg. **28:** 40–48, January 1946.

Osteomata and osteochondromata of the pelvic bones are usually considered to be benign growths, but they may become malignant. Some, but not all, are accessible to surgical removal. Complete eradication can be determined only by microscopic examination. The patient usually seeks relief for pain, swelling, or deformity caused by the tumor. About 10 per cent of these lesions can be expected to recur after removal.

In the authors' series of 40 patients with osteochondromata of the innominate bone, 26 were males and 14 females, and the age range was four to sixty-two years. Three patients with multiple congenital exostoses are included. The duration of symptoms varied from one week to twenty-one years; in 3 cases the tumor was found incidentally.

Sixty-nine surgical procedures were carried out on 40 patients, one patient being operated upon 12 times. Eleven patients received postoperative irradiation, but no definite evidence of benefit from the irradiation could be determined.

Nine, or 22.5 per cent, of the 40 patients are known to be dead. Eight, or 20 per cent, were living with recurrences at the time of the report. Recurrence is not, however, an absolute indication of malignancy. Four cases proved to be malignant. No evidence of mutation was found, but sections from one part of the tumor may be benign while other sections are malignant.

JOHN B. MCANENY, M.D.

Eosinophilic Granuloma of Bone. Report of a Case. J. O. Mercer. New Zealand M. J. **44:** 320–322, December 1945.

Eosinophilic granuloma is a variant of the presumably infective diseases of the reticulo-endothelial system, of which Hand-Schüller-Christian disease, infective reticulo-endotheliosis, and Letterer-Siwe's disease are more familiar examples. The majority of these conditions are rapidly fatal. One group, however, usually shows little systemic disturbance and the lesions resolve after curetting, radiotherapy, or even spontaneously. These latter cases were first described as solitary granuloma of bone but more recently, since they have been found to be multiple in some instances and carry a characteristic histologic picture, have been more accurately termed eosinophilic granuloma of bone. This disease closely simulates malignant disease of bone, particularly myeloma, both clinically and in microscopic appearance. Because of the vast differences in prognosis, it is important to distinguish the two.

The patient described in this report was a girl first seen at the age of nineteen months with a fluctuant bluish swelling immediately behind the anterior fontanelle, near the vertex of the skull. Radiologic examination showed a circular punched-out defect in the upper part of the right parietal bone. Three months later, the defect had enlarged to some extent and measured 1 1/4 × 1 1/2 inches. One year after the first observation, signs of acute mastoiditis developed. At operation, the bone of the mastoid area was found to be soft, and a considerable portion of the middle ear was filled with what appeared to be a vascular tumor. A section was taken but no definite diagnosis was obtained. After showing satisfactory healing, the mastoid scar broke down in about six weeks, and it was again necessary to explore the area. At this time, extensive bone destruction was found, and the antrum and middle ear were full of new growth. Microscopic examination suggested chronic osteomyelitis or eosinophilic granuloma of bone. The child made rapid progress following this exploration and any further surgical intervention was considered unwarranted. Two years later, the parietal tumor was found to be slowly resolving, and a radiograph of the skull showed reduction in the size of the bony defect. As far as can be determined from the report, no radiation therapy was given and healing of the parietal lesion was spontaneous.

BERNARD S. KALAYJIAN, M.D.

Backache. Henry W. Meyerding and Forrest L. Flashman. J. A. M. A. **130:** 75–78, Jan. 12, 1946.

Attention is called to a fairly common spinal lesion responsible for low back pain; namely, a defect in the pars interarticularis or isthmus of the vertebra which is known as prespondylolisthesis, spondylolysis, rachischisis, and spondyloschisis. Trauma is considered the precipitating factor, with a congenital lesion as the predisposing factor.

Patients complain of backache of several years' duration with aggravation in direct proportion to the amount of strain placed on the back. Examination may or may not elicit pertinent signs. The diagnosis depends on a careful history and roentgen examination. The importance of the oblique projection for demonstration of the defect is emphasized.

Treatment is directed toward increasing the stability of the lower spine. The majority of patients have been treated conservatively, by back supports, rest, sleeping on a firm bed, application of heat and massage to the back, and exercises to strengthen the muscles of the back. Those who did not respond to conservative treatment have improved following spinal fusion.

Reproductions of roentgenograms and reports of seven cases are included. H. D. WELSH, M.D.
(University of Michigan)

Pyogenic Osteomyelitis of the Spine. Differential Diagnosis Through Clinical and Roentgenographic Observations. Jose Puig Guri. J. Bone & Joint Surg. **28:** 29–39, January 1946.

This study is based on 48 cases of osteomyelitis of the vertebral body or arch, which are divided as to location and nature of the infection.

The *hip-joint syndrome* presents a septic reaction with hip-joint pain, but there is no pain on palpation of the posterior aspect of the articulation nor on percussion of the trochanter. Motion is limited only in extension. Tenderness is confined to a region of the spine, with limitation of motion of the spine especially in flexion and spinal pain on any attempt to extend the leg.

In the *abdominal syndrome*, the symptoms are suggestive of intra-abdominal disease, but in the presence of a vertebral lesion contraction of the abdominal muscles during palpation causes no change in the pain or tenderness, while in abdominal disease the pain practically disappears. One case in the author's series presented this syndrome.

The *meningeal syndrome* shows clinical signs of meningeal irritation. The onset may be acute or insidious. Three such cases were seen.

The *back-pain syndrome* may be acute, subacute, or insidious. In the acute form (16 cases) there is sudden back pain, severe, constant, and usually interfering with sleep. There is a marked systemic reaction. Blood culture may be positive. An abscess may form after one to three weeks. The subacute form (7 cases) shows a mild toxemia, often following a septic infection elsewhere in the body. Epidural abscess may form, with a flaccid paralysis of the lower extremities, temperature elevation, and difficulty in voiding. With an insidious onset, there is no general systemic reaction; the sharp pain is not relieved by rest, but, in fact, is worse at night and upon sneezing and coughing. There is localized tenderness and limitation of motion.

Roentgenographically there is no distinctive feature of pyogenic osteomyelitis of the spine. The localized form showed a small circumscribed area of destruction near the epiphyseal ring or cartilaginous plate. Narrowing of the intervertebral space and atrophy of the bone occur early. After four to six months, sclerosis appears. Healing takes place in nine to twelve months.

It is only by careful study of films taken at intervals over a long period of time that the difference between pyogenic and tuberculous osteomyelitis will become evident. In the tuberculous type the duration is much longer—two to three years as compared to nine to twelve months. The intervertebral space is narrowed in pyogenic infection but not to the same degree as in tuberculosis. New bone formation is seen in one to three months in pyogenic infection, but much later, if ever, in tuberculosis. Sclerosis develops early about a pyogenic infection but is absent or very mild in an early tuberculous infection.

In the diffuse form, lessening of density and fuzziness of outline occur early and at about three months are followed by sclerosis that lasts for three to six months. In tuberculous spondylitis, the atrophy lasts for at least two years and is rarely replaced by sclerosis. Reactive new bone formation is rare and late in tuberculosis but early and constant in pyogenic infection.

Very infrequently bone sclerosis is seen in tuberculosis but is certainly rare and usually only defined in radiographs of the pathological specimens. Sclerosis in pyogenic spondylitis is clearly seen and is a differential feature. Spondylitis characterized by marked sclerosis and bone formation should be suspected of being chronic staphylococcic osteomyelitis.

JOHN B. MCANENY, M.D.

Fracture of the Medial Epicondyle with Displacement into the Elbow Joint. James Patrick. J. Bone & Joint Surg. **28:** 143–147, January 1946.

Fracture of the medial epicondyle with displacement into the elbow joint usually occurs between the ages of 10 and 17, and is often associated with injury to the ulnar nerve. It may result from a fall on the hand with abduction of the forearm on the humerus or it may follow a posterolateral dislocation of the elbow. Diagnosis is usually made by x-ray, although the patient cannot always extend the elbow, and the displaced epicondyle may be overlooked. Ulnar nerve paralysis suggests injury to the medial epicondyle and its location should be determined. Reduction may be effected by abduction of the forearm with supination and extension of the wrist and fingers, which pulls the epicondyle from the joint space.

In studying this problem the author finds that, if in a lateral view of the elbow the epicondyle can be seen at the level of the joint, it may be considered to be in the joint. A strong faradic current applied to the flexor muscles with the wrist held in extension may pull the displaced epicondyle from the joint space.

In old cases, it is often impossible to move the epicondyle. Operative removal has been rather unsatisfactory, because the rough surface of the epicondyle erodes the coronoid process and initiates an arthritic process, which is not corrected by removal of the fragment. The author believes it better not to operate on these patients, since some cases will clear up in time and in any event little good can be done surgically.

Ulnar nerve paralysis usually clears up if given enough time. Sometimes a constricting fibrous band must be removed. Anterior transplantation of the ulnar nerve may be necessary where a cubitus valgus deformity is present, which stretches the nerve.

JOHN B. MCANENY, M.D.

Pneumoroentgenarthrography as a Diagnostic Aid in Internal Derangements of the Knee. John B. Butts and John T. Mitchell. U. S. Nav. M. Bull. **46:** 77–82, January 1946.

In a series of 50 cases of injury to the knee in which pneumoroentgenography was carried out, 24 patients were operated upon and the roentgen diagnosis was verified in 18 (75 per cent). The authors believe that air as a contrast medium for x-ray visualization has a definite value in the diagnosis of injuries to the semilunar cartilages, in hypertrophic synovitis, in hypertrophy of the retropatellar fat pad, and in the establishment of a differential diagnosis in cases of persistent or recurrent synovitis or hemarthrosis. A 40-inch distance (tube-film) with vertical (long axis of knee) tube shift of 2 1/2 inches for the stereo films was employed; one lateral and both anteroposterior (dorso, ventral) and postero-anterior stereo projections were made, with the rays paralleling the tibial articular surface. With careful positioning, 5 × 7-inch films were used in par speed cassettes. Results with the Potter-Bucky diaphragm were somewhat more satisfactory than with a non-grid technic. Roughly from 60 to 140 c.c. of air was necessary to separate the tissues properly and fill the joint space, depending upon the size and habitus of the patient, intercommunication and size of the bursae, presence of small amounts of fluid, and other factors. The procedure should be used only in patients with suspected injury or damage to non-radiopaque structures within the knee, in whom a clinical diagnosis cannot be made. It should never be carried out on an acutely inflamed joint.

A Review of 18 Cases of Arthrotomy of Knee Joints. Lowell I. Thomas. Mil. Surgeon **98:** 20–24, January 1946.

Eighteen cases of knee disability which came to operation are analyzed. A closer scrutiny of the preoperative roentgenograms, with the operative findings in mind, revealed that damage to cartilaginous articular surfaces may be anticipated when changes in subchondral bone density are found on the film.

Although x-rays of the knees are usually characterized by their "negativity," occasionally serial comparative films of both knees will demonstrate changes in density of subchondral bone, indicating articular surface damage. The outline of the normal femoral condyles and the normal shallow notches in the anterior surfaces of the femoral condyles can be distinguished from the abnormal, roughened, decalcified, indistinct articular surface outlines. This information is of considerable diagnostic value and is useful, with postoperative films, in checking the progress over a long period of time.

Fractures in Electroshock Therapy as Related to Roentgenographic Spinal Findings. James H. Huddleson and Hirsch L. Gordon. Mil. Surgeon **98:** 38–39, January 1946.

Roentgenograms of the spine were taken of all but 9 of the first 252 psychotic patients receiving electric shock therapy at one Veterans' Facility. One hundred and forty spines were normal, the other 103 showed abnormalities of varying degree. One patient had an old pre-shock spinal fracture. Excluding this case, 13 vertebral and 3 other fractures occurred in the series. The fracture rate for normal spines was 4.3 per cent and for the abnormals 6.8 per cent, a difference of 2.5 per cent, which the authors consider statistically insignificant. There was thus no relation between abnormalities seen in pre-electroshock spinal roentgenograms and shock-induced fractures.

Orthoroentgenography as a Method of Measuring the Bones of the Lower Extremities. William T. Green, George M. Wyatt, and Margaret Anderson. J. Bone & Joint Surg. **28:** 60–65, January 1946.

Under certain conditions it is necessary to determine the exact length of the bones of the lower extremities. Any method of doing this should meet certain requirements. (1) It should be sufficiently accurate to record the comparative true length at any one examination. (2) The precision of measurement should remain constant for varying bone lengths, in order to compute accurately the true increment of growth. (3) Sufficient detail should be delineated to show abnormalities and the epiphyseal lines.

The method described here consists of three separate exposures of the lower extremities on a cassette 14 by 48 inches, centering over the three joints successively. Sliding lead plates protect two segments of the film while the third is being exposed. A lead marker is used to center the x-ray tube over the joint and to check the accuracy of the exposure. The extremities are held immobile by tapes during radiography.

Comparison of this method of measurement of long bones with others shows its great advantage and accuracy. The length can be measured directly from the films without any correction factors.

JOHN B. MCANENY, M.D.

GYNECOLOGY AND OBSTETRICS

Uterosalpingography. C. M. Spangler. Surg. Clin. North America. **25:** 1340–1344, December 1945.

In 1914 Rubin attempted to visualize the uterine and fallopian tubes, using collargol. This medium was abandoned due to its irritant action on the peritoneum. In 1925 Fosdike employed lipiodol. This has subsequently fallen into disrepute for the following reasons: (1) accidental injection of vessels into which the oil penetrated, (2) oil embolism, (3) non-absorption of the oil from the peritoneal cavity, and (4) acute peritonitis with abscess formation. Subsequently diodrast, skiodan, and uroselectan were utilized in the hope of overcoming the objections offered by the oily medium. These, however, lack the viscosity for a constantly satisfactory hysterosalpingogram. Titus utilized acacia in skiodan to increase the viscosity of the watery medium. The choice of substance utilized, however, is less important than the care and technic of administration.

Uterosalpingography is employed (1) to demonstrate congenital abnormalities of the uterus and fallopian tubes; (2) to show the location of uterus and fallopian tubes in relation to other pelvic masses; (3) to outline the contour and content of the uterine cavity; and (4) for the localization of the site of tubal obstruction which has been previously established by repeated Rubin tests. The latter is the procedure in which uterosalpingography is of most value.

Contraindications include (1) acute vaginitis, endocervicitis or any acute pelvic infection; (2) inflammatory pelvic masses; (3) menstruation; (4) pregnancy, whether uterine or extra-uterine; and (5) cardiovascular, pulmonary, and other serious systemic disease.

ELLWOOD W. GODFREY, M.D.

Double Uterus and Double Vagina. Identical Doubles Demonstrated by Colpohysterosalpingography. R. R. Killinger and H. B. McEuen. Am. J. Obst. & Gynec. **51:** 121–124, January 1946.

The authors advocate a simple and uniform nomenclature for describing abnormalities of the female genital tract due to lack of fusion of the müllerian ducts and/or irregularities of canalization. Such a classification has been published by Taylor (Am. J. Obst. & Gynec. **46:** 388, 1943) and is as follows: (1) uterus arcuatus, (2) double uterus with a single cervix, (3) septate uterus with a single or septate vagina, (4) double uterus with a double cervix, (5) uterus with a rudimentary horn or absence of one horn. Taylor estimated that one out of 1,500 obstetric cases and one in about 2,000 gynecologic cases show this type of deformity, while others place the incidence still higher. Its practical significance has been brought out by Schauffler (J. A. M. A. **117:** 1516, 1941), who recorded a case in which a patient was seen by nine physicians and was "unnecessarily pounded, thumped, curetted, aborted and laparotomized, mainly because of a complete double uterus which presented diagnostic difficulties during pregnancy."

Helpful diagnostic signs are irregular menses, dyspareunia, repeated unexplained abortions, and repeated malposition of the fetus. The author believes that roentgen pelvimetry should be done routinely as an aid in diagnosis.

The case of a 24-year-old white woman with a double uterus and double vagina is reported. Examination revealed the presence of a complete septum in the vagina and two distinct cervices were palpable. A roentgenogram following injection of iodochloral showed the two cervices, two cervical canals, two separate uteri, and two tubes—one to each of the separate uteri—clearly outlined. HUGH A. O'NEILL, M.D.

Evaluation of Roentgen Pelvimetry. T. G. Stoddart. Canad. M. J. **54:** 50–52, January 1946.

During a recent twelve-month period, the author made a roentgen study of the pelvis in approximately 100 women. Each of these was referred for roentgen consultation, and none was examined as an ordinary routine procedure. In the majority dystocia was anticipated. The usual reasons for sending obstetrical cases to the x-ray department for pelvimetry are: (1) abnormal external and internal pelvic measurements; (2) a floating head at term; (3) a history of previous dystocia; (4) an elderly primipara; (5) suspected breech presentation; (6) medicolegal considerations.

The majority of this series were primiparae, and many had abnormal external measurements. Previous injury or disease of the lumbar spine and pelvis was also an indication for roentgen examination. One small group of patients had gone into labor before roentgen measurement was requested, but most of the women were ambulatory and able to cooperate fully. The examination was conducted at eight or eight and a half months in most instances, which is considered the optimum time.

The author uses a form of the Thoms method. In addition to a flat film of the abdomen and pelvis for general detail, he takes a lateral projection either with the patient erect or lying on her side. An 8 × 10 measuring film (for the lateral view) is then made, using the perforated lead grid located at a level corresponding to the mid-line of the sacrum. A final anteroposterior film is obtained with the patient semi-upright, supported on a canvas and wooden framework. Following the first exposure to outline the pelvis, a second exposure is made on this film with the perforated lead grid at the level of the inlet. This method has given very satisfactory results. The three films used for measurement permit a study of the pelvic contours as well, an important consideration, since abnormal contours may cause dystocia as readily as faulty measurements.

Complete parturition records were obtained for 72 patients. In 29 of these, approximately 40 per cent, cesarean section was done, for the following indications: disproportion (70 per cent), placenta praevia, uterine inertia and non-engagement of the head after trial labor, maternal systemic disease, breech presentation with limited pelvic capacity, toxemia, and spinal deformity or ankylosed hip.

The author's conclusions from this study are that pelvic roentgen measurements are desirable in all cases where dystocia is anticipated; that the study of the pelvic contours is to be stressed; that the optimum type of pelvis is the round or gynecoid, while the least desirable for normal childbirth is the true flat type or platypelloid. BERNARD S. KALAYJIAN, M.D.

Roentgenological Visualization of the Sacral Hiatus During Late Pregnancy. Paul A. Bishop. Surg. Clin. North America **25:** 1391–1393, December 1945.

For visualization of the sacral hiatus in late pregnancy, Bishop advocates an anteroposterior Bucky film. The pelvis is tilted slightly by placing a pillow under the patient's knees. The tube is adjusted 25 inches above the table top and centered at the level of the anterior-superior spine. It is then shifted caudalward 17 inches and tilted cephalad at a 45-degree angle.

The film shows the shape, width, and length of the sacral hiatus as well as any secondary openings or windows above the hiatus. A description of the latter is important in caudal anesthesia since the tip of the needle follows the posterior wall of the caudal canal. Should the tip of the needle penetrate the soft tissue of a "window," the injection would be made outside the canal and anesthesia would be unsatisfactory.

ELLWOOD W. GODFREY, M.D.

Roentgenological Visualization of the Placenta. Paul A. Bishop. Surg. Clin. North America **25:** 1394–1407, December 1945.

By soft-tissue technic the placenta may be visualized in a vast majority of cases when 50 per cent or more of it lies above the pelvic inlet. Two lateral films are made. The first is centered over the middle of the posterior third of the fundus to record the posterior wall; the second is centered over the anterior third and the exposure is made sufficiently light to show the anterior wall. An anteroposterior film is also made with the patient lying flat on her back. With proper technic, the subcutaneous fat layer of the fetus will appear as a black line. Between this fat line and the periphery of the uterus there are four structures of the same density, the uterine wall, the skin of the fetus, the placenta, and the amniotic fluid. The first two are uniformly thin. The placenta will displace the fetal soft parts, while this is not true of amniotic fluid.

Identification of the placenta in the fundus rules out placenta praevia as a cause of uterine bleeding. The accuracy of such a negative diagnosis should be better

than 97 per cent with films of satisfactory quality. Marginal implantation is suggested as a possibility whenever the main portion of the placenta is visualized on the lower half of the uterus. The degree of marginal implantation may be important in the clinical management of the case. Because of the wide variation of size and shape of the placenta, however, this point cannot be judged by the amount of placenta that is visible in the soft-tissue films, but should be based on the relationship between the fetal head and maternal bladder. In order to study this, the bladder is distended with 125 to 200 c.c. of 5 to 10 per cent solution of intravenous urographic medium and stereoscopic anteroposterior films are made. In addition, if no placental shadow is identified in the abdominal portion of the uterus or if there is a low implantation, the fetal head may be displaced from the pelvic wall, giving further localizing information.

ELLWOOD W. GODFREY, M.D.

THE GENITO-URINARY SYSTEM

A Pyelographic Sign in the Diagnosis of Perinephric Abscess. Douglas T. Prehn. J. Urol. **55:** 8–17, January 1946.

In the diagnosis of perinephric abscess there is no syndrome or pathognomonic sign which can be solely relied upon. In the history, trauma and previous infections, especially boils, carbuncles, and osteomyelitis, are especially important.

The roentgenographic signs to look for are as follows: *In the plain film:* (1) Obscuration or obliteration of the lateral border of the psoas muscle shadow; (2) obscuration or obliteration of the kidney shadow; (3) obscuration of the ribs or transverse processes or both; (4) curvature of the spine with the convexity away from the abscess; (5) the abscess shadow; (6) displacement of the colon by the abscess; (7) displacement, fixation, diminution or limitation of the excursion of the diaphragm.

In the intravenous urogram and retrograde pyelogram: (1) Renal fixation; (2) anterior displacement of the kidney; (3) outward displacement of the kidney and inward displacement of the ureter, best seen on stereoscopic films; (4) rotation of a calyx in the upper pole of the kidney when the abscess lies posterior and medial to the upper pole.

One case is reported in which the last named sign was present.

J. L. BOYER, M.D.

THE BLOOD VESSELS

The Superior Vena Cava Syndrome: Report of Thirty-Five Cases. Hugh Hudson Hussey, Sol Katz, and Wallace M. Yater. Am. Heart J. **31:** 1–26, January 1946.

The syndrome of obstruction of the superior vena cava is produced by any condition which interferes with the flow of blood through that vessel without a corresponding interference with blood flow through the inferior vena cava. The principal symptoms and signs of the syndrome are edema and cyanosis in the upper part of the body, dyspnea, and dilated veins indicative of the collateral circulation. Other symptoms may be present depending on the nature of the underlying cause. The main causes are aneurysm of the ascending aorta, bronchiogenic carcinoma, malignant lymphoma, and carcinoma with metastases to the mediastinum. Simple thrombosis of the superior vena cava is rare. Phlebography and measurement of venous pressures are the only procedures by which the diagnosis can be confirmed during life. The site of the obstruction can be demonstrated by phlebography. In the presence of obstruction the venous pressure in the upper extremities is significantly higher than that in the lower.

The authors' findings are based on a study of 35 cases; in 27 the causes were verified, and in 8 they were uncertain. Of the verified lesions, 12 were aneurysms of the ascending aorta, of which 2 had perforated into the superior vena cava, 6 were bronchiogenic carcinomas, 5 were malignant lymphomas, 2 were acute lymphocytic leukemia, 1 was a hypernephroma metastatic to the mediastinum, and another was a carcinoma of the ovaries with mediastinal metastases. Mediastinal masses were demonstrated roentgenographically in 4 of the 8 unverified cases. In the other 4 cases, there were no roentgen evidences of a mediastinal tumor and no clinical features to suggest the cause of the syndrome.

The venous pressure was measured in the antecubital vein in 34 of the 35 cases, and found to be 300 mm. or more of saline in 20, and 400 mm. or more in 12. In 6 cases it was below 200, a figure which might have been accepted as normal, had not the pressure in the femoral vein been very much lower.

Phlebograms were made in 13 cases, with diodrast or thorotrast, the injections being either in one or both antecubital veins or the external jugular vein. Several case histories and illustrations are included in the article.

In 2 cases of aortic aneurysm the superior vena cava syndrome was produced by communication between the aneurysm and the superior vena cava. This condition should be suspected when the syndrome develops explosively in a patient with aneurysm of the aorta. The usual features of arteriovenous communication, such as thrill, bruit, and an increase in pulse pressure, may not be present.

HENRY K. TAYLOR, M.D.

Vasokymography in Research for the Demonstration of Vascular Flow. M. Zehnder. Schweiz. med. Wchnschr. **76:** 29–30, Jan. 12, 1946.

In addition to arteriography of the brain, the author made a kymographic study of the vessels during the contrast filling in order to determine the type and direction of blood flow. This enhances the value of the study, especially if the lesion proper does not happen to be demonstrated on the film. Its principal usefulness is in arteriovenous aneurysm and in tumor.

LEWIS G. JACOBS, M.D.

Terminal Aortography in Obliterative Arteritis. Bonte, Vandecastelle, and Desruelle. J. de radiol. et d'électrol. **26:** 209–213, 1944–45.

The authors describe the injection of one of the organic iodides, as used in pyelography, into the abdominal aorta to determine the patency of the femoral artery, or to localize the block when no pulsation is felt in the vessel itself. They hope thus to aid the neurosurgeon in determining whether or not he wishes to attack the sympathetic supply of the vessel, and in selecting the point of attack.

From the standpoint of bedside surgery, this would appear a bit far-fetched, particularly when one sets off against the possible benefits accruing from the procedure the possible hazards involved.

Perhaps the best appraisal of what the authors have to offer may be had by quoting the legends of several of their illustrations:

"Fig. 3: Involuntary injection into the right renal artery. The injection was too high, and the needle sunk too obliquely . . . because of the passage of fluid into the right kidney, the injection of the external iliacs is insufficient."

"Fig. 4. A poor terminal aortography. The injection at the usual site was done without success; this is understandable when one considers the sinuosity of the aorta, which deviates to the left. This too high injection did opacify the superior mesenteric and the renals . . . ."

"Fig. 5: Endarteritis of the left iliacs. The left and external iliacs have irregular borders and an inconstant caliber, due to endarteritis. . . ."

"Fig. 6: Obliteration of the common iliac at its termination. On the left, due to the development of a sacral branch (middle), a meshwork of collateral vessels has been established to compensate . . . ."

Other illustrations are in series, showing various alterations in the primary anatomical arrangement of the vessels springing from the bifurcation.

Several observations occur to one: First, in each case there is evidence of a collateral circulation. Then, no surgical application of such findings as there are is made clear. Certain it is, that no competent neurosurgeon would predicate a procedure upon the mere visualization or failure of visualization of some arterial branch in a preparation of this sort; as the authors themselves admit, if less than the proper amount of dye is injected, the lower branches will not be satisfactorily visualized.

Furthermore, the authors' statement that aortic puncture is without risk is not impressive. Atheromatous aortas, degenerated, sometimes strip their coats one from the other without external trauma; likewise a few large needle punctures, close together, through hard calcific plaques, might easily initiate a freely bleeding wound of the vessel wall (and the authors make it plain that they have to try more than once with the needle in some of the cases).

All in all, this procedure would seem to be one destined for limbo. Clinicians of good judgment want no part in procedures which are inexact and misleading and which in addition constitute a menace to the patient.

PERCY J. DELANO, M.D.

RADIOTHERAPY

Diagnosis and Management of Uterine Carcinoma and Sarcoma. Lewis C. Scheffey. Surg. Clin. North America **25:** 1262–1280, December 1945.

Malignant growths of the pelvis represent the gravest of gynecologic disorders. The most frequent site is the uterus. Carcinoma is commonest and the cervix is most often affected, the portio chiefly and the mucosa of the canal infrequently. Next in order is fundal involvement. Sarcoma is relatively infrequent.

In some instances there may be no objective symptoms of cervical cancer. Because of this, periodic pelvic examinations offer hope and opportunity for early diagnosis.

The treatment of carcinoma of the cervix, whether by irradiation or surgery, is chiefly controversial in one respect—the management of the supposedly early case. When reasonable doubt exists that the cancerous growth is no longer limited to the confines of the cervix, and irrespective of possible lymphatic metastasis, there should be no hesitancy in selecting irradiation in preference to a primary surgical procedure.

In the Jefferson Clinic, in existence since 1921, with a follow-up of 98 per cent, no surgical procedures have been employed since 1923. The relative five-year survival rate of those patients treated solely with irradiation, according to groups, is as follows: Group I, 75.0 per cent; Group II, 43.3 per cent; Group III, 22.1 per cent; Group IV, none; Group V, 13.3 per cent. The relative survival rate for "early" cases (Groups I and II) has been 47 per cent, while the over-all rate for the entire series is recorded as 23.5 per cent. The primary mortality was 1.3 per cent in a series of 285 patients; there was no primary mortality among the Group I and II cases. These figures are believed to compare favorably with the purely surgical survival rates reported, although they are inferior to the results of Lynch's combined radium and surgical procedure, with the exception of his primary mortality, which was 5.4 per cent.

At the Jefferson Clinic, from which this report comes, preliminary x-ray therapy has been regularly employed before radium application since 1936, and since 1942 a transvaginal port has been used in addition to the four external ones. The roentgen factors are 25 ma. at 200 kv., 0.5 mm. or 1.0 mm. copper and 1.0 mm. aluminum filtration, 50 cm. skin-target distance, ports 16, 19, or 20 cm. square. Two ports are treated daily, each receiving 200 r (in air). The treatments are continued until a well marked erythema is obtained, which in general will occur with a total of 1,600 to 2,400 r to each portal. After the external portal treatment is well under way, the transvaginal port is utilized until a similar total dose has been obtained. After two to four weeks, depending upon the patient's reaction, she is returned to the hospital for radium therapy. Two or three 50-mg. capsules of radium screened by 1.5 mm. of platinum enclosed in rubber tubing, are arranged in tandem in the uterine cavity and cervical canal. Then ten 10-mg. needles, 2 cm. active length, each screened with 0.5 mm. of platinum, are placed interstitially about the periphery of the growth, at the junction of the supposedly involved and sound tissue. Each radium element used is attached individually by strong string to a gauze strip which is firmly packed into the vagina and fornices, thoroughly displacing the radium-containing tissue away from the normal vaginal epithelium, the bladder, and the rectum. A retention catheter is left in the bladder. An average dose of 4,500 to 5,000 mg.-hr. is given. Nearly all Group IV patients, and occasionally Group III patients, receive x-ray therapy only.

Carcinoma of the cervical stump following supravaginal hysterectomy has an incidence perhaps in the neighborhood of 1 per cent. In relation to carcinoma of the cervix in general, the incidence is higher, averaging 4 to 5 per cent from collected statistics. The consensus is that cervical stump cancer is best treated with irradiation.

Carcinoma of the cervix complicating pregnancy

occurs approximately once in 10,000 times. It is the opinion of the author that management of the carcinoma should have precedence over the possibility of securing offspring, and that complete irradiation therapy should be used.

When the possibility of a fundal cancer is present, diagnostic curettage should always be resorted to promptly. The concept of treatment of such lesions most widely accepted at the present calls for a combination of irradiation and surgery. In the Jefferson Clinic from 1921 to 1929 patients were either treated by surgery alone or by irradiation alone. Because of the relatively low survival rate of patients treated solely with surgery, the plan of treatment was gradually changed, preliminary irradiation with radium being employed increasingly before surgery was attempted. X-ray therapy after radium, or after surgery preceded by radium, is used only if there is visual or palpable evidence of pelvic extension at operation.

If supravaginal hysterectomy has been employed in sarcoma of the uterus, with or without adnexal conservation, the outlook is dubious because of possible involvement of the retained structures. In such instances, postoperative irradiation, with radium applied to the cervical stump and x-ray therapy to the pelvis, is imperative. ELLWOOD W. GODFREY, M.D.

Histologic Study of the Effect of Irradiation on Adenocarcinoma of the Endometrium. Lyman M. Stowe. Am. J. Obst. & Gynec. **51:** 57–66, January 1946.

This study is reported because the author feels that the evaluation of radium therapy has for the most part been based on clinical results in terms of five- or ten-year cure rates, or increase in survival rates, and little attention has been paid to the correlation of these results with histologic findings. His observations were made in 53 cases of adenocarcinoma of the body of the uterus in which the diagnosis was established by curettage prior to irradiation. The histologic material consisted of pan-hysterectomy and bilateral salpingo-oophorectomy specimens obtained five weeks after the completion of radiation therapy.

All patients received radium irradiation. In 7 the radium was applied in two or three capsules arranged in tandem in a long straight applicator. The dose varied from 2,000 mg. hr. to 4,900 mg. hr. In the remaining 46 instances a jointed tandem applicator was used, with 3 or 5 capsules in series, with a platinum wall 1 mm. thick. In the usual 5-capsule set-up, 4,500 to 5,000 mg. hr. of radiation was delivered. Twenty-three patients had deep x-ray therapy prior to operation as well as radium.

In order to make sure that no carcinoma was overlooked, the entire endometrium, together with the musculature underlying it to a depth of 0.7 to 1.0 cm., was removed and sections were made at intervals of not more than 3 mm. at right angles to the surface.

A 50.9 per cent incidence of residual tumor was found. In 10 cases where x-ray was employed in adequate dosage together with radium irradiation, the incidence of residual tumor fell to 40 per cent, while in a larger series where radium alone was used the incidence was 56.5 per cent. However, the author indicates that this difference is not statistically significant. In the majority of instances where residual carcinoma was found it was in the uterine musculature.

The conclusion is reached that surgical attack must be considered to be the essential feature of curative therapy in the treatment of adenocarcinoma of the corpus uteri. It is still possible that preliminary irradiation may be useful as additional therapy or for palliation. RUSSELL WIGH, M.D.

Indications for Roentgen Therapy of Bladder Carcinoma. Recognition of Suitable Cases. Franz Buschke and Simeon T. Cantril. Surg., Gynec. & Obst. **82:** 29–35, January 1946.

This paper deals primarily with roentgen therapy from a curative point of view. In the treatment of those cancers of the bladder which are considered incurable by surgical or radical radiological procedures because of the extension of the disease or the general condition, radiation therapy with the purpose of palliation only has no place. It is useless and in many instances harmful. It increases the discomfort of the patient and discredits radiation therapy.

Curative roentgen therapy may be attempted with most hope of success in papillary carcinomas with a moderate degree of differentiation and without marked invasion of the bladder wall. In general the carcinoma should not have extended through the wall of the bladder; no metastases should be present, and the strength of the patient should be sufficient to support the course of therapy planned. Adequate urinary drainage must be established, and no severe infection should be present. An enlarged prostate or an occluding tumor should be removed before treatment is instituted. Prior suprapubic operations lower the possibility of adequate irradiation.

If an extensive carcinoma recurs following fulguration, or if recurrence appears likely to the operator, roentgen therapy should be instituted promptly if it is to be used at all.

Small lesions of a primarily infiltrating type are better treated by excision. If such a lesion is so located that complete bladder resection is the only surgical procedure possible, interstitial irradiation is probably superior to roentgen therapy, provided the invasive tumor is less than 3.5 cm. in diameter.

No details of therapy are supplied except that treatment is given daily for six to eight weeks through three portals, at 800 kv. Of 69 patients treated from 1934 to 1943, 10 were well, 55 were dead or alive with active disease, and 4 were lost from follow-up at the time this study was made.

This is the authors' third report on supervoltage therapy of carcinoma of the bladder (for the others, see Supplement to the Staff Journal of the Swedish Hospital, Seattle, May 1941, No. 2, p. 77; J. Urol. **48:** 368, 1942). They still consider their experience "too young to make final conclusions," and regard the observations set forth here as "only a working basis for further investigation."

FREDERICK A. BAVENDAM, M.D.

Hodgkin's Disease. VII. Treatment and Prognosis. Henry Jackson, Jr., and Frederic Parker, Jr. New England J. Med. **234:** 103–110, Jan. 24, 1946.

The treatment of Hodgkin's paragranuloma, due to its localized nature, may be either excision of the nodes or excision followed by irradiation. Both procedures have shown good results.

In Hodgkin's granuloma, there is no specific treatment. Biopsy should precede therapy, and a complete

examination, including a chest film, should be made. Irradiation with 200 kv., 0.5–1. 0 mm. copper filtration, 100–200 r daily for a total depth dose of at least 500 r, should be prescribed. Supervoltage irradiation has not been used sufficiently long to determine its value. Treatment should be given cautiously in the presence of large mediastinal masses and evidence of an acute infection. Unexplained fever, abdominal pains, a persistently elevated white count, and generalized itching suggest involvement of the abdominal or para-aortic nodes. Bone lesions are usually less sensitive to radiation than other lesions, but even here irradiation often is of value, at least for relief of pain. Transfusions, general care, and surgery are often necessary. Aspirin in large doses will usually control bone pain.

Hodgkin's sarcoma is very resistant to irradiation. In most cases the disease arises in the internal organs or retroperitoneal nodes and, as a result, is often not discovered until very late.

The prognosis of Hodgkin's paragranuloma is not entirely discouraging. Of 26 patients, 54 per cent lived five years or more, and 5 have survived 15 years. Of the 12 who died, 5 succumbed to unrelated diseases, and 7 to Hodgkin's granuloma.

Hodgkin's granuloma usually leads to death in one to three years. Thirteen per cent of the authors' patients lived five or more years. An acute infectious onset usually indicates death within six months. With pulmonary involvement death is to be expected in three to eight months.

The prognosis in Hodgkin's sarcoma is poor. No patient in this series lived more than three years; 60 per cent died within two years.

JOHN B. MCANENY, M.D.

Treatment of Leukemia with Radioactive Phosphorus. R. Feissly. Schweiz. med. Wchnschr. **76:** 8–9, Jan. 5, 1946.

The treatment of leukemia with radioactive isotopes depends on three factors: (1) the possibility of selective introduction into the leukemic tissues; (2) the possibility of injection in non-toxic form; (3) the possibility of injection without depositing the substance in other organs in sufficient quantity for its radioactivity to be dangerous.

P^{32}_{15}, producing beta radiation, has been shown to meet these requirements. After discussing the literature, the author reports the case of a 60-year-old man with lymphatic leukemia who had become radiation-fast. Five millimicrocuries of radiophosphorus were injected as sodium phosphate (pH 7.4), leading to a reduction of the white cells from 112,300 to 80,000 per c.mm. in ten days, in spite of the minute dose. The patient suffered no ill effects. LEWIS G. JACOBS, M.D.

BENIGN AND NON-NEOPLASTIC DISEASE

Indications and Contraindications in the Irradiation Therapy of Benign Uterine Conditions. George A. Hahn. Surg. Clin. North America **25:** 1306–1312, December 1945.

In contrasting irradiation with surgery for benign uterine conditions, Hahn states that there are differences which are at once apparent. Economically irradiation is more desirable. External irradiation does not require hospitalization, while the patient who is being treated with local radium is ordinarily sent home after about a week's stay. The expense of an intrauterine radium application or fractional x-ray treatments is much less than that of a longer hospital stay following major uterine surgery with its attendant anesthesia, operating room, and professional fees.

In patients with vaginal bleeding, the presence of carcinoma must first be considered. Diagnostic curettage must always be performed prior to irradiation therapy, or carried out at the time of the intended radium application. ELLWOOD W. GODFREY, M.D.

Use of Radium in the Aerotitis Control Program of the Army Air Forces. A Combined Report by the Officers Participating. Ann. Otol., Rhin. & Laryng. **54:** 650–724, December 1945.

Aerotitis, due to inability to ventilate the middle ear during flight, has been a major cause of disability in flying personnel. A program to reduce the incidence of aerotitis in the Army Air Forces was instituted in 1944. The attack was based primarily on the elimination of the most common cause of eustachian tube malfunction, namely, hyperplastic lymphoid tissue in the nasopharynx. Irradiation of such tissue with radium was chosen as the best and most practical method of treatment for the desired purpose. The technic was that developed by Crowe (see Burnam and Crowe: Mississippi Valley M. J. **67:** 109, 1945. Abst. in Radiology **47:** 208, 1946). Two nasopharyngeal applicators, each containing approximately 50 mg. of radium sulfate, are inserted in the nasopharynx for 8.5 minutes, giving a dose of 1 gm. 25 seconds (in the earlier cases the period was slightly less, with a correspondingly decreased dose).

The present report is based on studies conducted on flying personnel in the European and Mediterranean Theatres of Operation, by medical officers attached to the Eighth, Twelfth and Fifteenth Air Forces, and in the United States to the First and Third Air Forces. All of the officers engaged in the program were otolaryngologists who were specially trained in the use of the nasopharyngoscope and in the technic of nasopharyngeal irradiation.

Every patient selected for treatment had hyperplastic lymphoid tissue in or about the eustachian tube orifices. Overseas, only the patients with a history of aerotitis or ear-ventilating difficulties were treated.

A total of 14,345 men were examined by the participating units and 6,881 were selected for treatment. The total number of treatments given was 14,045. Not a single instance of burn or ulceration of the nasopharyngeal or the nasal mucous membrane occurred in the 14,045 treatments given. A small proportion of the men had a mild stuffiness of the nose, a slight sore throat, or a sensation of a head cold after treatment.

Of 636 men with a history of recurrent aerotitis, 74 per cent had less difficulty ventilating their ears during flight and 89 per cent had a marked decrease in the amount of nasopharyngeal lymphoid tissue when examined with a nasopharyngoscope, thirty days or more after the third treatment. Seventy men, or 11 per cent, showed no reduction in the amount of lymphoid tissue in the nasopharynx, and 165 men, or 26 per cent, had no subjective improvement.

The beneficial effect of prophylactic irradiation was shown by the drop in incidence of aerotitis in 778 men after high altitude flights.

The principal cause of failure to improve after irradiation treatments was the presence of a large mass of adenoids. For such patients, surgical removal, supple-

mented by irradiation, would have been more effective. In other patients various factors, such as nasal allergy, chronic sinusitis, and psychologic reactions, were found to be contributing causes for the lack of improvement.

Basic precautions were adopted to protect medical personnel and patients from overexposure to radiation. For those giving the treatments, the principal safety measure was distance. Except when placing or removing the applicators from the nasopharynx, all personnel remained at a distance of 20 feet or more. No evidence of overexposure, either of patients or of irradiation clinic personnel, was noted by any of the participating officers.

In conclusion, the use of the nasopharyngeal radium applicator is a safe, practical, and effective method of irradiating hyperplastic lymphoid tissue in the nasopharynx. In addition, irradiation of hyperplastic lymphoid tissue about the eustachian tube orifice is an effective prophylactic measure for aerotitis in flying personnel. STEPHEN N. TAGER, M.D.

Irradiation of the Eustachian Tube. An Anatomic, Physical and Clinical Study of a Treatment for Recurrent Otitis Media Applied to Aero-Otitis. Edmund P. Fowler, Jr. Arch. Otolaryng. **43:** 1–11, January 1946.

A series of 80 airmen who had been grounded because of recurrent aero-otitis were treated by the application of radium or radon to the eustachian tube; 46 of these were returned to full flying duty. Since only 66 of the patients could be regarded as properly selected, treated, and followed, this represents a 69 per cent cure rate.

This brief report of results is preceded by a consideration of the anatomy and pathology of the eustachian tubes, illustrated with photomicrographs, and is followed by a discussion of the method of application. Particular emphasis is laid upon the importance of filtration. The author discusses the use of brass, platinum, and Monel metal. With platinum all the beta radiation is filtered out, but with Monel metal the radiation is mixed, beta and gamma. A table is included showing the doses in roentgens for 50 mg. radium at various depths for the different filters, with different dosage times. No final conclusions as to the procedure of choice are reached.

The author mentions the possibility of using high-voltage roentgen therapy if neither radon nor radium is available. While special applicators are to be preferred, radium capsules designed for other purposes can often be adapted for insertion into the nasopharynx. The treatment is without danger in the hands of a competent radiotherapist. It not only gives successful immediate results but it forestalls the deafness which develops sooner or later from the recurrent attacks of otitis media which are almost an inevitable sequel to malfunction of the eustachian tubes.

[See also article on this subject by the same author, Arch. Otolaryng. **40:** 402, 1944. Abst. in Radiology **45:** 210, 1945.]

Case of Brucellosis Cured by Teleroentgen Therapy. J. Aimard. J. de radiol. et d'électrol. **26:** 369, 1944–45.

In this article, the author attempts to convince the reader that in a case of Malta fever, by a series of treatments at a meter and a half distance, using 25 to 50 r at a seance, he materially aided the convalescence of his patient. Indeed, he puts it more strongly than that, saying: "Under the influence of this treatment, as one may establish by the temperature curve, the defervescence began. . . ." Anyone familiar with Malta fever knows, of course, that the temperature occasionally declines quite by itself. In short, the author has failed entirely to establish the cause and effect relationship which he assumes. PERCY J. DELANO, M.D.

Effect of X-Rays on Leishmania Tropica in Vitro. B. Feldman-Muhsam and L. Halberstaedter. Brit. J. Radiol. **19:** 41–43, January 1946.

On the flagellate form of *Leishmania tropica* cultivated *in vitro*, 1,250,000 r were immediately lethal. At 500,000 r some were immobilized, the proportion increasing as the dose was raised. A dose of 150,000 r destroyed the capacity for multiplication in the culture medium. The immediately lethal dose for the Donovan bodies could not be determined.

In the clinical treatment of leishmaniasis favorable results are obtained with 300 to 600 r repeated three or four times at weekly intervals. It is therefore apparent that the clinical benefit is not due to a direct effect on the parasite. SYDNEY J. HAWLEY, M.D.

APPARATUS

A Feed-Back Amplifier for Ionization Currents. Frank T. Farmer. Brit. J. Radiol. **19:** 27–30, January 1946.

The construction of an intensity meter using a small chamber on a flexible cable is described which will measure from 1 to 50 r per minute. By using a large negative feed-back the effective time constant of the input circuit is reduced to a small fraction of its normal value and a linear response to radiation intensity is produced. SYDNEY J. HAWLEY, M.D.

Design of Filters to Produce "Flat" X-Ray Isodose Curves at a Given Depth. A. E. Chester and W. J. Meredith. Brit. J. Radiol. **18:** 382–385, December 1945.

Flattening of the isodose curves for given depths was accomplished by making stepped filters thickening toward the center. This was done only for long narrow fields. Change in dose distribution along the short axis of the field did not occur. SYDNEY J. HAWLEY, M.D.

EFFECTS OF RADIATION

Subtotal Replacement of the Skin of the Face for Actinodermatitis Due to Roentgenotherapy: With Multiple Areas of Squamous Cell Carcinoma. Hilger Perry Jenkins. Ann. Surg. **122:** 1042–1048, December 1945.

The patient whose history is recorded here had received x-ray therapy to the skin of the face some fifteen years previously for a pustular dermatitis. Twenty-five treatments had been given, mostly within a four-month period, but the dosage is not noted. Except for a burn from the treatments, the patient experienced no trouble until about twelve years later, when weeping lesions appeared which became crusted over and ulcerated. At the time of his first appearance before the

author, there was an extensive scarring of the skin of the face and multiple small squamous-cell epitheliomas developing in the scarred areas. Some cervical lymph node enlargement was present. The enlarged nodes were removed surgically and found to contain metastatic carcinoma. Despite this, the skin of the entire face was removed in stages and replaced by grafted skin. The details of the procedure are clearly outlined by the author. The end-result was excellent. The main purpose of this article is to demonstrate what can be done in the way of extensive replacement of the skin of the face following roentgen-ray reaction and development of carcinoma. BERNARD S. KALAYJIAN, M.D.

Carcinoma Subsequent to the Radiotherapeutic Menopause. James A. Corscaden, John W. Fertig, and S. P. Gusberg. Am. J. Obst. & Gynec. **51:** 1–12, January 1946.

The authors discuss here a follow-up series of 1,108 patients in whom an artificial menopause had been induced because of benign uterine bleeding, fibromyomata, or one of a few other benign conditions. Thirty-six cancerous growths were found in various parts of the body, 15 of which were in the uterus.

Some patients had been kept under observation for twenty-five years, but the general average was 6.7 years. Based on modified statistics, the same number of women in the general population, during the same length of time, should contract 4.4 carcinomas of the uterus. The observed number of cases, therefore, is 3.4 times as large as the expected number. There is not a corresponding excess of cancers in other organs.

Of the 15 uterine tumors, 9 involved the corpus and 6 the cervix. This abnormal preponderance of carcinoma of the corpus is in agreement with that present in other reported series, in which the ratio is 2 of the corpus to 1 in the cervix. It is inferred that the endometrium of uteri which bleed abnormally prior to the menopause is predisposed to the subsequent development of carcinoma.

The authors present several tables showing the length of follow-up, cases of non-uterine cancer subsequent to radiation therapy, death rates per 100,000 females from carcinoma and other malignant tumors, etc.

PHILIP W. DORSEY, M.D.

Laryngeal Cancer Following Roentgen Therapy. D. den Hoed. Acta radiol. **27:** 20–22, Jan. 31, 1946. (In German.)

Cancer of the larynx developed in two middle-aged persons twenty-five years after heavy roentgen irradiation of the throat. No other etiological factors were present and the author believes that there is some connection between the irradiation and the development of the cancer.

Histological Effects of Radiophosphorus on Normal and Lymphomatous Mice. W. S. Graff, K. G. Scott, and J. H. Lawrence. Am. J. Roentgenol. **55:** 44–54, January 1946.

The effects of radiophosphorus (P^{32}) were studied by use of a transmissible lymphoma in mice. Some of the mice were injected intravenously with 1.2×10^7 lymphoma cells, while others were used as controls. Thirteen days after inoculation, some of the mice were given 1.0 c.c. of an isotonic solution of sodium phosphate intravenously which contained 195.3 microcuries of P^{32} per cubic centimeter. Some of the control animals received a similar dose of P^{32} at the same time. Twelve other mice received a similar injection of lymphoma cells and seven days later half of these animals received four 1.0 c.c. subcutaneous injections (54.5 microcuries per cubic centimeter) at two-hour intervals. Four normal animals received similar P^{32} injections and 2 others were kept as controls.

The results showed an initial depressing action of P^{32} on the lymphocyte series in the peripheral blood stream. After four days, when the granulocytes begin to drop off markedly, there already was an increasing deposition of P^{32} in bone. The retention of P^{32} in bone is of much longer duration than in lymphatic or any other tissue. There is no direct evidence that the neoplastic cells are more radiosensitive than other cells. It was found that, at corresponding stages in the lymphomatous process, the treated animals had less infiltration of organs by leukemic cells than the non-treated groups. In both the normal and leukemic animals, the greatest drop in white blood cells occurred during the first four days after administration of P^{32}. The chief cell type to be affected is the lymphocyte and the lymphoma or leukemic cell. During the following five days the rate of drop diminishes, but during this period the greatest decrease in granulocytes occurs.

Studies of the exchange of P^{32} in leukemic tissues of mice revealed a higher uptake than in other soft tissues. This greater uptake in neoplastic tissue is of interest, since these cells receive relatively more radiation.

Even though there is some selective irradiation, especially by virtue of P^{32} localization in infiltrated lymph nodes, spleen, and liver, one eventually faces the same problem as when using spray or local roentgen irradiation, since the whole marrow, and therefore both leukemic and normal elements, are being irradiated. These predominant effects of P^{32} on the various elements of marrow constitute the limiting factor in its use in the therapy of leukemia and make it of doubtful value in lymphosarcoma and allied diseases. The general problem is to find a radio element or compound of the element which would localize to a high degree in or immediately around the neoplastic cell. Since leukemia is such a diffuse disease, the possibilities of discovering a method of true selective irradiation are not great, and for this and other reasons we must look for the control of this disease by some other method.

CLARENCE E. WEAVER, M.D.

Studies on the Effects of Radioactive Sodium and of Roentgen Rays on Normal and Leukemic Mice. Titus C. Evans and Edith H. Quimby. Am. J. Roentgenol. **55:** 55–66, January 1946.

Radioactive sodium, at the present time the most readily prepared of all radioactive substances, does not concentrate in any organ or group of organs, but instead is, within a short time after its administration, distributed throughout the extracellular fluids of the body. It emits penetrating beta and gamma rays. Its half-life, 14.8 hours, is long enough to be useful and yet short enough so that dosage can be closely correlated with effect.

Normal mice were injected with amounts of radioactive sodium varying from 150 to 4,000 microcuries. Other normal mice were exposed to doses of from 350 to 1,000 r of roentgen rays, 70 per cent of the dose being administered one day and 30 per cent the next. The effects of the two treatments were found to be of the same kind. Similar changes were produced in the

differential counts. Lymphocytes were more radiosensitive than the other leukocytes. In animals with leukemic adenopathy, injections of radioactive sodium produced severe leukopenia, usually of short duration. In general, such animals showed more reduction in lymphocyte number than was produced by comparable amounts of radiation in controls. Estimations of distribution of radioactive sodium in various organs and tissues of sacrificed animals showed that there was no considerable concentration of the material in any particular organ or tissue.

The results presented indicate that the effects produced by subcutaneous injection of radioactive sodium are of the same sort as those resulting from whole body roentgen irradiation. It was estimated that 10 microcuries per gram of body weight will produce the same general effect as 100 r of roentgen rays. It is emphasized that this equivalence is applicable only to mice, not to larger animals or to man. In man, this amount would give a much higher dose of radiation for two reasons. In the first place, whereas in the mouse practically no gamma radiation is effective, and only about three-fourths of the beta radiation, in man practically all the beta rays and a considerable portion of the gamma rays are absorbed. Furthermore, the mouse eliminates about a third of the material in three days, while in this period the average human being excretes less than 10 per cent. It is estimated that the "equivalent roentgens" from a given dose per gram of body weight in man would be at least twice as much as in a mouse. No evidence of selective concentration of the radioactive sodium in the lymph nodes was found.

CLARENCE E. WEAVER, M.D.

Biological Effects of Penetrating Radiations. A Review. F. G. Spear. Brit. M. Bull. **4:** 2–11, 1946. **Comparative Studies of the Biological Effects of X Rays, Neutrons and Other Ionizing Radiations.** L. H. Gray. Ibid. pp. 11–18. **Genetic Effects of Radiations.** D. G. Catcheside. Ibid. pp. 18–24. **Action of Radiations on Viruses and Bacteria.** D. E. Lea. Ibid. pp. 24–26. **Quantitative Histological Analysis of Radiation-Effects in Human Carcinomata.** Alfred Glucksmann. Ibid. pp. 26–30. **Measurement of Radiation.** G. J. Neary. Ibid. pp. 30–35. **Total Energy-Absorption in Radiotherapy.** Frank Ellis. Ibid. pp. 36–43. **On Technical Methods in X-Ray Therapy.** J. Read. Ibid. pp. 43–49. **On Technical Methods in Radium Therapy.** S. Russ. Ibid. pp. 49–51. **Million Volt Therapy.** G. S. Innes. Ibid. pp. 51–58. **Protective Methods in Radiology.** W. Binks. Ibid. pp. 58–64.

The first number of Volume 4 of the *British Medical Bulletin* is devoted to radiobiology in its experimental and practical aspects. It comprises the papers listed above, most of which are in the nature of reviews.

EXPERIMENTAL STUDIES

Studies on the Brown-Pearce Rabbit Carcinoma with the Aid of Radioactive Isotopes. A. Forssberg and F. Jacobsson. Acta radiol. **26:** 523–534, Nov. 30, 1945.

Since the Brown-Pearce rabbit carcinoma produces tumors in about 80 per cent of animals grafted and the course of development of the tumor and metastases is rapid, it is possible to maintain a relatively high level of radioactivity during the critical period of growth of the tumor by injection of radioactive phosphorus (P^{32}). The author first established the distribution of radioactive isotope in the organs of normal animals; the kidneys, liver, spleen, and adrenals were found to contain greater amounts per gram of weight than other organs. Rabbits having the tumor were then injected with the phosphorus at varying intervals after grafting, and recordings of the amount of radioactivity as measured by a Geiger-Müller counter in comparison with known standards were made on metastatic tissue and on the uninvolved portions of various organs.

The resulting data showed no significant difference between organs from normal rabbits and the uninvolved portions of the corresponding organs from rabbits dying with the tumor. However, the metastatic tissue, regardless of the organ in which it originated, showed a high and essentially equal amount of retained phosphorus of the order of magnitude of normal kidney, liver, spleen, or adrenal. Excretion likewise followed a curve similar to that for the organs of higher metabolic rate. Although concentration in the metastatic tissue was high, it was somewhat greater in the rapidly growing portions of the tumor than in the older necrotic portion. Extractions of preparations of tumor cells indicated greater phosphorus retention in the nucleoprotein fraction in the rapidly growing portion of the tumor, but greater retention in the acid-soluble fraction in necrotic tissue.

The authors conclude that it would probably not be possible to treat metastases without damage to normal tissue. However, they suggest the possibility of early treatment to prevent metastases and plan experiments along that line. ELIZABETH A. CLARK, M.D.

Length and Width Changes in the Pulmonary Arterial System of Rabbits in Passing from the Stage of Expiration to That of Collapse as Revealed by Roentgenography. Charles C. Macklin. Dis. of Chest **11:** 590–595, November-December 1945.

The author has previously set forth his view that with vigorous ventilation there is change in the length and width of the pulmonary arteries and veins: they increase with inspiration and decrease with expiration (Tr. Roy. Sc. Canada, vol. 39). This periodic change in the volume of blood in the pulmonary vessels rhythmically repeated, he believes, has the effect of a pump which aids the heart. Roentgen studies of rabbits show that in passing from expiration to collapse there is a similar reduction in the length and width of the arteries and veins. In a unilateral pneumothorax, the blood flow is lessened, while compensatory emphysema with an increase in the size of the pulmonary vessels occurs in the contralateral lung, so that the circulation is maintained. Two roentgenograms are included showing the comparative size of the vessels in moderate inflation and collapse in rabbit lungs filled with latex which had been opacified with thorotrast.

HENRY K. TAYLOR, M.D.